DISSERTATION ON

A PROSPECTIVE RANDOMIZED CONTROLLED STUDY COMPARING THE SERUM CORTISOL LEVELS IN PATIENTS ADMINISTERED GENERAL ANAESTHESIA VERSUS SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERIES

Dissertation submitted in partial fulfillment
of the regulations for the award of the degree of

M.D. DEGREE, BRANCH – X
ANESTHESIOLOGY

Of

TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

ESIC- MEDICAL COLLEGE & POSTGRADUATE INSTITUTE OF MEDICAL SCIENCE AND RESEARCH,
KK NAGAR, CHENNAI- 78.

APRIL 2016

ENDORSEMENT BY THE DEAN/
THE HEAD OF THE INSTITUTION

This is to certify that this dissertation titled "**A PROSPECTIVE RANDOMIZED CONTROLLED STUDY COMPARING THE SERUM CORTISOL LEVELS IN PATIENTS ADMINISTERED GENERAL ANAESTHESIA VERSUS SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERIES."** submitted by **DR. PRAVEEN KUMAR G**, appearing for M.D Degree Branch – X ANAESTHESIOLOGY examination in April 2016 is a bonafide record of work done by him in partial fulfillment of the regulations of Tamil Nadu Dr. M.G.R Medical University, Chennai. I forward this to the Tamil Nadu Dr. M.G.R Medical University, Chennai Tamil Nadu, India.

DEAN

Dr. SRIKUMARI DAMODARAM,

M.S., M.Ch (SGE), M.A.M.S.,

F.A.C.S., F.I.C.S., F.M.M.C

ESIC Medical College and PGIMSR

K.K. Nagar, Chennai – 78.

DATE:

PLACE: K.K. Nagar

CERTIFICATE BY THE HEAD OF DEPARTMENT

This is to certify that dissertation entitled "**A PROSPECTIVE RANDOMIZED CONTROLLED STUDY COMPARING THE SERUM CORTISOL LEVELS IN PATIENTS ADMINISTERED GENERAL ANAESTHESIA VERSUS SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERIES"** is a bonafide research work done by **Dr. PRAVEEN KUMAR G,** in partial fulfillment of the requirement for the degree of M.D. in Anesthesiology

Signature

DATE:

PLACE: KK Nagar

Prof. S. Gayathri, M.D., D.A
Professor& HOD
Department of Anesthesiology
ESIC MC& PGIMSR
K.K Nagar, Chennai- 78

BONAFIDE CERTIFICATE

This is to certify that the dissertation named "**A PROSPECTIVE RANDOMIZED CONTROLLED STUDY COMPARING THE SERUM CORTISOL LEVELS IN PATIENTS ADMINISTERED GENERAL ANAESTHESIA VERSUS SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERIES"** is a bonafide work performed by **DR. PRAVEEN KUMAR G**, postgraduate student, Department of Anesthesiology, ESIC Medical college & PGIMSR, Chennai – 78, under my guidance and supervision in fulfillment of regulations of The Tamil Nadu Dr. M.G.R Medical University for the award of M.D. Degree during the academic year 2013 – 2016.

GUIDE:

Dr. K. Radhika, M.D.,
Associate Professor,
Department of Anesthesiology,
ESIC Medical College & PGIMSR,
Chennai –78.

CO-GUIDE:

Dr. Ilango Ganesan, M.D.,
Associate Professor,
Department of Anesthesiology,
ESIC Medical College & PGIMSR,
Chennai–78.

DECLARATION

I solemnly declare that this dissertation entitled "**A PROSPECTIVE RANDOMIZED CONTROLLED STUDY COMPARING THE SERUM CORTISOL LEVELS IN PATIENTS ADMINISTERED GENERAL ANAESTHESIA VERSUS SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERIES"** has been conducted by me at ESIC Medical College & PGIMSR, Chennai, under the guidance and supervision of **Dr. RADHIKA, M.D. and Dr. ILANGO GANESAN, M.D.,** Department of Anesthesiology, ESIC Medical College & PGIMSR, Chennai. This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the University regulations for the award of the degree of **M.D. Branch X (Anesthesiology).**

Date:

Place: Chennai **(DR. PRAVEEN KUMAR G)**

ACKNOWLEDGEMENT

In the first place, I would like to convey my gratitude to our Dean, **Dr. SRIKUMARI DAMODARAM M.S., M.Ch., M.A.M.S.,F.A.C.S., F.I.C.S., F.M.M.C** for providing me unflinching encouragement and support .

I would also like to thank **PROF. KAMALINI SRIDHARAN, M.D., D.A,** former HOD, Department of Anesthesiology, ESIC MC & PGIMSR for her immense support and encouragement for the study.

I would also like to thank **DR. K. RADHIKA, MD. ,** Associate Professor, my guide and mentor, who had been instrumental in the completion of this study and for her supervision, advice, giving me moral support throughout the work.

I would also like to thank **Dr. ILANGO GANESAN, M.D.,** Associate Professor, my co-guide and mentor, who had been instrumental in the completion of this study and for his supervision, advice, giving me moral support throughout the work.

I am extremely thankful to **DR. MADHUBALA MD.,** Associate Professor, Department of Biochemistry and **DR THUTHI MOHAN M.D**., Department of Biochemistry who had been the backbone of this thesis. They saw to that investigation kits were always available and the tests reported promptly without any delay.

I am grateful in every possible way to the Assistant professors, Specialists, Medical Officers, Senior Residents and the postgraduates of the Department of Anesthesiology for helping me to conduct the study in the theatre.

Many sincere thanks to the department of community medicine, in particular to the statistician **DR.ARUNA PATIL, Ph.D.,** for her guidance regarding the sample size and data analysis.

I am thankful to the Institutional Ethical Committee for their guidance and approval for this study.

I also thank the theatre personnel and biochemistry technicians for their help. I would like to thank all the patients for their participation and cooperation.

I am also thankful to my parents for their unconditional love and support

DR. PRAVEEN KUMAR G

CERTIFICATE OF APPROVAL

To

Dr. Praveen Kumar G,
PG in Department of Anesthesia,
ESIC Medical College & PGIMSR,
KK Nagar, Chennai-78.

Dear Dr. Praveen Kumar G,

The Institutional Ethical Committee of ESIC Medical College & PGIMSR reviewed and discussed your application for approval of the proposal entitled "**A Prospective Randomized controlled study comparing the serum cortisol levels in patients administered general anaesthesia versus supraclavicular brachial plexus block for upper limb surgeries**" at ESIC Medical College & PGIMSR, K K Nagar, Chennai 600 078, No. **13/27/10/2014**.

The following members of the Ethical Committee were present in the meeting held on 27.10.2014 conducted at ESIC Medical College & PGIMSR, KK Nagar, Chennai-78.

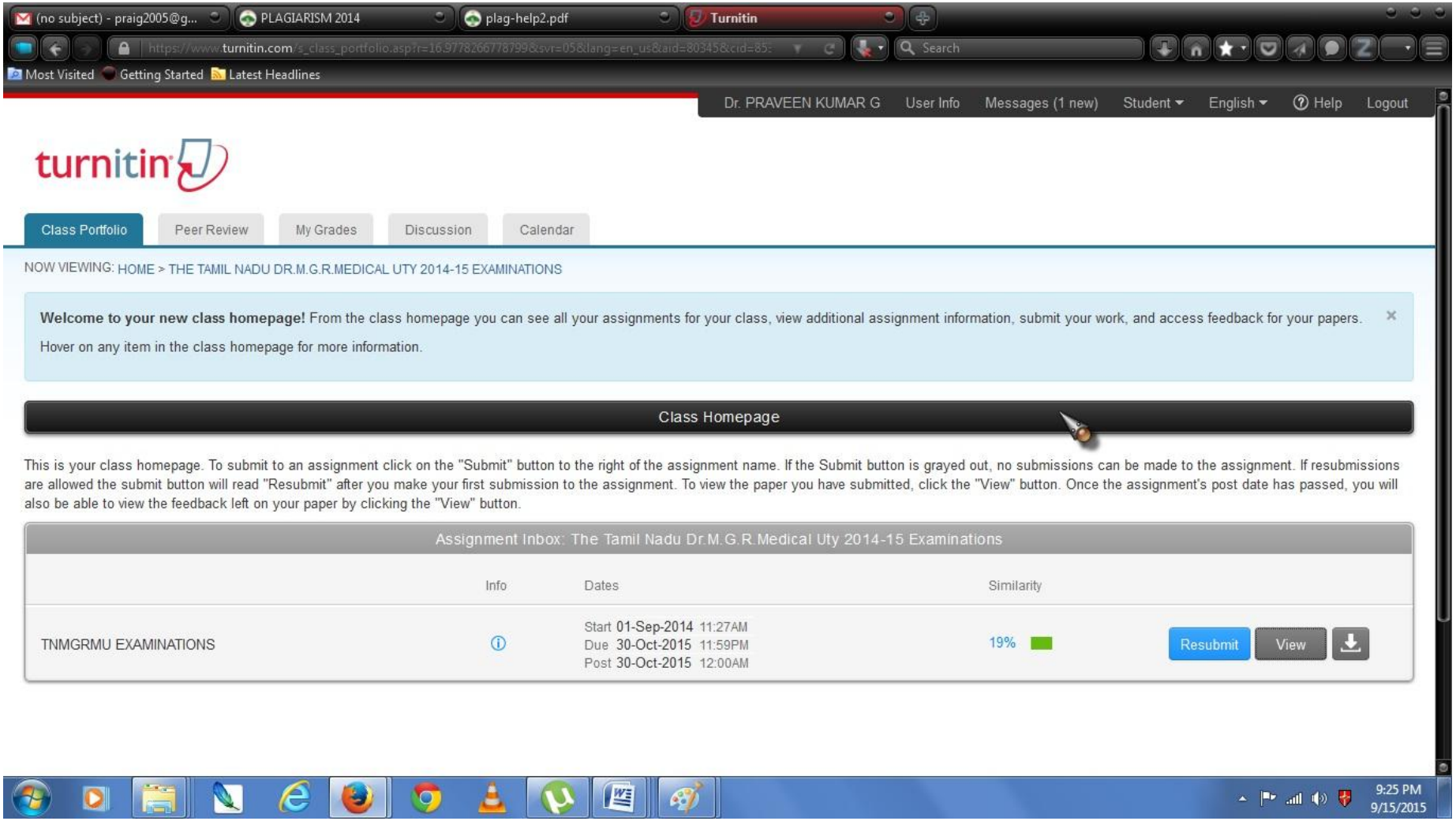
S.No.	ETHICAL COMMITTEE MEMBERS
1.	Prof. A.V. Srinivasan, Chairperson, EC Member EMERITUS Professor, The Tamilnadu Dr. MGR Medical University Former Prof. & HOD., of Institute of Neurology, Madras Medical College
2.	Prof. V. Rajalakshmi, Vice Principal, ESIC Medical College & PGIMSR, EC Member
3.	Prof. M. Kanaheswari, Medical Superintendent, ESIC Medical College & PGIMSR, EC Member
4.	Prof. Kamalini Sridharan, Registrar, ESIC Medical College & PGIMSR, EC Member
5.	Prof. S. Seethalakshmi, Prof. & HOD, Department of Pharmacology, ESIC Medical College & PGIMSR, EC Member
6.	Prof. S. Malliga, Prof. & HOD, Department of Biochemistry, ESIC Medical College & PGIMSR, EC Member
7.	Prof. Sowmya Sampath, Prof. & HOD, Department of Paediatrics, ESIC Medical College & PGIMSR, EC Member
8.	Prof. Usha Kothandaraman, Prof. & HOD, Department of Anatomy, ESIC Medical College & PGIMSR, EC Member
9.	Dr. Aruna Patil Bholenath, Assistant Professor, Department of Community Medicine, ESIC Medical College & PGIMSR, EC Member
10.	Dr. A. Sundaram, Dept. of Medicine [Diabetologist], EC Member
11.	Dr. O.L. Naganath Babu, Dept. of Surgical Gastroenterology, EC Member
12.	Dr. S. Dhanalakshmi, Dept. of OBG, EC Member
13.	Dr. Rajkumar Williams, Dept. of Surgery, EC Member
14.	Prof. C. Rajendiran, Department of General Medicine, EC Member
15	Dr. C.V. Aravindan, Scientist, EC Member
16.	Shri. K M Venugopal, Advocate, EC Member

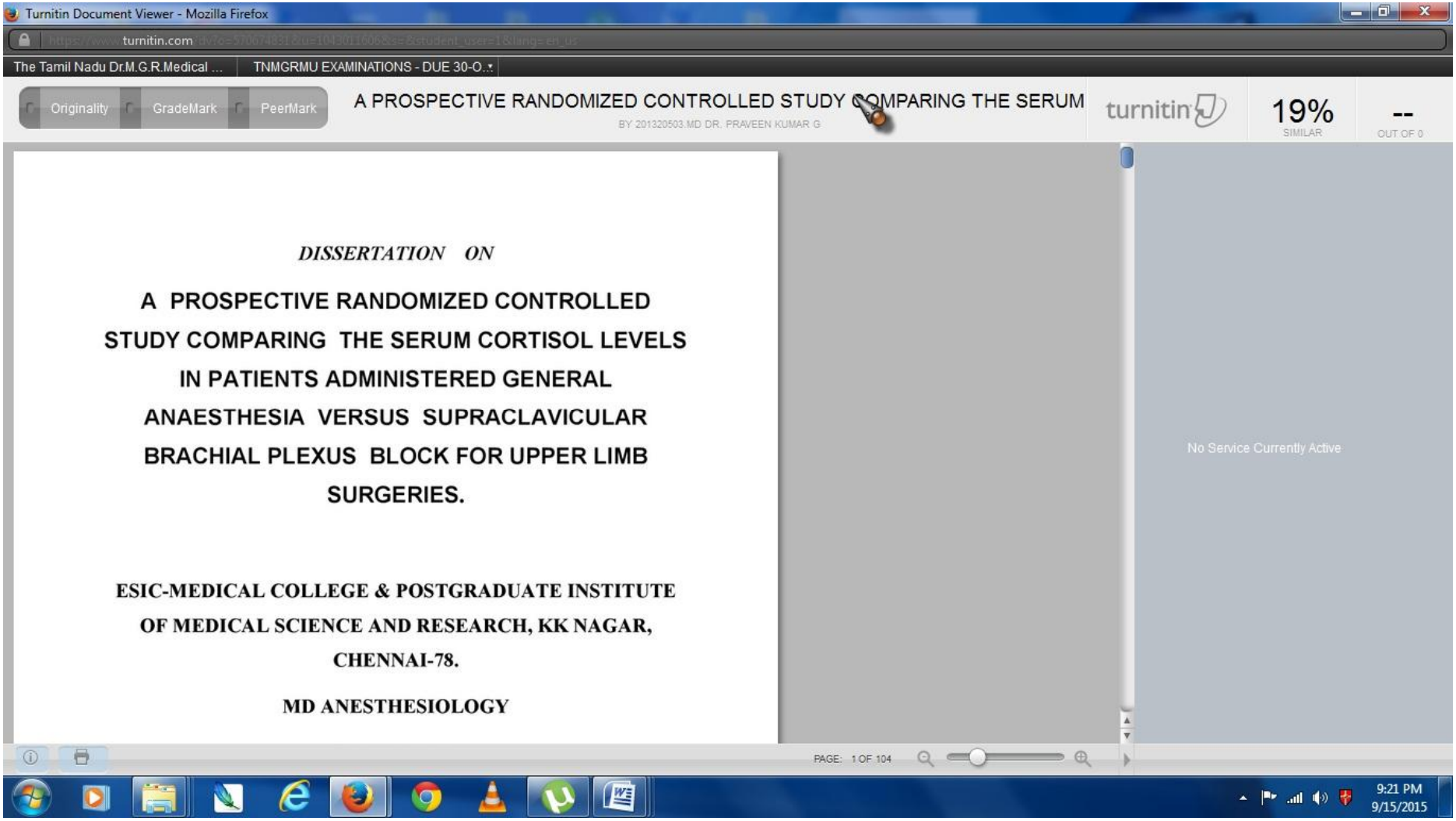
The proposal is approved to be conducted in its presented form.

The Institutional Ethical Committee expects to be informed about the progress of the study and significant adverse effects occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

[DR. A.V. SRINIVASAN]
CHAIRPERSON
ETHICAL COMMITTEE

Date : 27.10.2014
Place : Chennai 78


(no subject) - praig2005@g...
PLAGIARISM 2014
plag-help2.pdf
Turnitin
https://www.turnitin.com/s_class_portfolio.asp?r=16.9778266778799&svr=05&lang=en_us&aid=80345&cid=85:
Search
Most Visited
Getting Started
Latest Headlines
Dr. PRAVEEN KUMAR G
User Info
Messages (1 new)
Student
English
Help
Logout
turnitin
Class Portfolio
Peer Review
My Grades
Discussion
Calendar
NOW VIEWING: HOME > THE TAMIL NADU DR.M.G.R.MEDICAL UTY 2014-15 EXAMINATIONS
Welcome to your new class homepage! From the class homepage you can see all your assignments for your class, view additional assignment information, submit your work, and access feedback for your papers.
Hover on any item in the class homepage for more information.
Class Homepage
This is your class homepage. To submit to an assignment click on the "Submit" button to the right of the assignment name. If the Submit button is grayed out, no submissions can be made to the assignment. If resubmissions are allowed the submit button will read "Resubmit" after you make your first submission to the assignment. To view the paper you have submitted, click the "View" button. Once the assignment's post date has passed, you will also be able to view the feedback left on your paper by clicking the "View" button.
Assignment Inbox: The Tamil Nadu Dr.M.G.R.Medical Uty 2014-15 Examinations
Info
Dates
Similarity
TNMGRMU EXAMINATIONS
Start 01-Sep-2014 11:27AM
Due 30-Oct-2015 11:59PM
Post 30-Oct-2015 12:00AM
19%
Resubmit
View
9:25 PM
9/15/2015


Turnitin Document Viewer - Mozilla Firefox
turnitin.com
The Tamil Nadu Dr.M.G.R.Medical ...
TNMGRMU EXAMINATIONS - DUE 30-O..
Originality
GradeMark
PeerMark
A PROSPECTIVE RANDOMIZED CONTROLLED STUDY COMPARING THE SERUM
BY 201320503.MD DR. PRAVEEN KUMAR G
turnitin
19%
SIMILAR
--
OUT OF 0
DISSERTATION ON
A PROSPECTIVE RANDOMIZED CONTROLLED STUDY COMPARING THE SERUM CORTISOL LEVELS IN PATIENTS ADMINISTERED GENERAL ANAESTHESIA VERSUS SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERIES.
ESIC-MEDICAL COLLEGE & POSTGRADUATE INSTITUTE OF MEDICAL SCIENCE AND RESEARCH, KK NAGAR, CHENNAI-78.
MD ANESTHESIOLOGY
No Service Currently Active
PAGE: 1 OF 104
9:21 PM
9/15/2015

CONTENT

ABSTRACT

TITLE :

A PROSPECTIVE RANDOMIZED CONTROLLED STUDY COMPARING THE SERUM CORTISOL LEVELS IN PATIENTS ADMINISTERED GENERAL ANAESTHESIA VERSUS SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERIES.

SUBMITTED BY:

DR. PRAVEEN KUMAR G

GUIDE :

DR. K. RADHIKA, M.D.

CO- GUIDE :

DR. ILANGO GANESAN, M.D.

DEPT. OF ANESTHESIOLOGY

ESIC MC & PGIMSR

KK NAGAR

CHENNAI- 78.

EMAIL :

praig2005@gmail.com

BACKGROUND: Surgery is a stressful condition. It is associated with increased levels of catabolic hormones. The type of anesthesia has a great influence on the stress response. In general anesthesia, though the patient is paralysed the hypothalamus still receives signals from the surgical site, which results in activation of stress response. In regional anesthesia on the other hand there is complete blockade of impulses reaching the hypothalamus resulting in decreased activation of stress response. Ill effects of stress response include increased oxygen consumption, catabolism and altered immune functions. The adverse effects are associated with poor post operative course and clinical outcome. Cortisol is the most sensitive marker for stress response.

AIM: To compare the serum cortisol levels in patients administered general anesthesia versus supraclavicular brachial plexus block for upper limb surgeries

METHODS: This study is a prospective randomized controlled study. The study involved 62 patients, 1 patient was excluded from the study due to lysis of blood sample. The remaining 61 patients were divided into two groups, Group GA under general anesthesia with 30 patients and Group RA under supraclavicular brachial plexus block with 31 patients. In both the groups blood samples were taken at baseline, 30 minutes after skin incision, 3 hours after skin incision and 24 hours after skin incision for cortisol evaluation .

RESULTS: The preoperative cortisol levels in both the groups were comparable with P value of 0.398. At ½ hour the cortisol in Group RA was 4.30±1.59 mcg/ dl, in group GA was 23.32±14.71 mcg/dl. The cortisol values at 3 hours in group RA was 3.87±1.49 mcg/dl, in group GA was 21.16 ±12.75 mcg/ dl. The cortisol values at ½ hour and 3 hour was significantly low in Group RA when compared to Group GA with P value of 0.0001 in both the times. At 24 hours the cortisol values were comparable between the two groups with P value of 0.123.

CONCLUSION: From this study it was concluded that Cortisol levels at ½ hour and 3 hours after skin incision was significantly lower in Group RA when compared to Group GA. So the magnitude of stress response was significantly lower in RA group when compared to GA group as indicated by the cortisol level. So it can be concluded that supraclavicular brachial plexus block is better than general anesthesia for upper limb surgeries due to decreased stress response as indicated by the cortisol levels.

KEY WORDS: Cortisol, Stress Response, Supraclavicular Brachial Plexus Block, General Anesthesia

INTRODUCTION

Surgical procedures and injury are associated with a variety of stress responses. These stress responses have neurohormonal, metabolic and Immunological components. [(1)]

The patients posted for surgical procedure are anxious for many reasons. They are worried about anesthesia, the surgical procedure as well as post operative outcome. Pain also forms a part of the worry profile. These factors lead to stress and activation of the autonomic nervous system. During surgery the activation of the hypothalamus by the autonomic nervous system results in the increased release of nor-epinephrine from the pre synaptic terminal and epinephrine from the adrenal medulla. The activation of the hypothalamo-pituitary-adrenal axis causes an increased release of ACTH from the pituitary which in turn causes more release of cortisol. Increased secretion of cortisol is one of the key central features of neuroendocrine response to surgery.[(2)(3)]

In the past researches have shown that the magnitude of such a response depends upon the severity of injury, the operating time and the severity of postoperative pain. These endocrine and metabolic derangements have many adverse effects including increased oxygen

consumption, catabolism and altered immune functions. The adverse effects are associated with poor post operative course and clinical outcome

The type of anesthesia may affect the magnitude of such a stress response by modulating the pathophysiological pathways that produce neurohormonal and metabolic changes. By decreasing the operative stress we can improve the post operative outcome and we can reduce the duration of stay as well as the total cost of patient care[(4)]

The normally used opioids and inhalational agents do not suppress the stress response. High doses of opioids and inhalational agents on the other hand suppress the hypothalamus thus decreasing the activation of the neuroendocrine system. But these high doses are associated with delayed recovery, nausea, respiratory depression and other adverse outcomes. During regional anesthesia on the other hand there is blockade of both the afferents and efferent's leading to decreased stress response. [(1)(2)]

The aim this study is to compare the levels of cortisol between patients administered general anesthesia and supraclavicular brachial plexus block undergoing elective upper limb surgeries. Cortisol is used as a biochemical marker of the degree of stress response.

Aim of the Study

AIM OF THE STUDY

TO COMPARE THE SERUM CORTISOL LEVELS IN PATIENTS ADMINISTERED GENERAL ANESTHESIA VERSUS SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERIES

Objective of the Study

PRIMARY OBJECTIVE

COMPARISON OF STRESS RESPONSE IN PATIENTS ADMINISTERED GENERAL ANESTHESIA VERSUS SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERIES

Review of Literature

REVIEW OF LITERATURE

Charles Weissman[2] in his review article on 1990, describes that increased interest has been shown by the anesthetist on the stress response during surgery. He explained that major body injury, surgery or accident induces various metabolic, hormonal and immunological changes. These responses are associated with changes in protein, fat and carbohydrate mechanism. Overall there is increased catabolism in the body leading to hyperglycemia, proteolysis, lipolysis. Also there is sodium and water retention in the body. The intensity of these changes depends upon the extent of injury.

A. M. Cruickshank, W. D. Fraser, H. J. G. Burns, J. Van Damme and A. Shenkin [5] in 1990, suggested that IL-6 is the activator of acute phase response that is seen during surgery and trauma. The macrophages at the site of injury produce cytokines like IL-1, IL-2, IL-6. This study compared the levels of IL-6 after surgeries of different magnitude. It was seen that maximum raise of IL-6 followed major surgeries. The study concluded that IL-6 is a sensitive marker of tissue injury, greater the surgical intensity greater was the IL-6 levels.

David L. Brown[6] in 1993 in his article “Brachial Plexus Anesthesia: An Analysis of Options” described the anatomy of brachial plexus and the various methods of achieving brachial plexus block. He described that supra clavicular brachial plexus block can be used to obtain anesthesia of the entire upper limb. However care should be taken while performing the block because of the chances of pneumothorax are high. When using nerve stimulator, an insulated needle should be used. The current should be approximately adjusted to about 3 milliamps and the needle should be directed towards the nerve so as to obtain muscle contractions between 0.5- 1 milliamps. Once the needle is in position a 1ml of local anesthetic is deposited through the needle which should abolish the muscle contraction.

In 1995 J. P. Barker, P. N. Robinson, G. C. Vafidis, J. M. Burrin, S. Sapsed-Byrne and G. M. Hall [7] did a study on 40 patients undergoing cataract surgery. 10 Non insulin dependent diabetes mellitus patient (NIDDM) under retro bulbar block, 10 NIDDM patients under general anesthesia, 10 non diabetic patients under retro bulbar block and 10 non diabetic patients under general anesthesia. They compared cortisol, blood sugar and insulin levels up to 4 hours after surgery. The results showed that in both general anesthesia groups (NIDDM and non

diabetics) the cortisol and blood sugars raised during the surgery while in both local anesthesia groups (NIDDM and non diabetics) there was no significant raise. Insulin levels increased in non diabetics according to the raised blood sugar but there was no raise in insulin levels in NIDDM patients. Thus they concluded that the metabolic control was better when the cataract surgery was done under local anesthesia when compared to general anesthesia.

In 2000 J. P. Desborough[(1)] described the various endocrine, metabolic and immunological changes associated with surgery. The stress response to surgery is characterized by a rise in the counter regulatory hormones (i.e. cortisol, glucagon, nor epinephrine, growth hormone, vasopressin). These hormonal changes produce increased catabolism which mobilizes substrates to provide energy. There is salt and water retention as well. He explained the effects of the type of anesthesia on the stress response with regional anesthesia causing less stress response when compared to general anesthesia. In general anesthesia large doses of opioids like morphine, fentanyl are necessary to reduce the stress response but such large doses cause respiratory depression and prolonged post op ventilation. In regional anesthesia on the other hand there is complete blockade of both the afferents and

efferents from the surgical site thereby inhibiting the afferents from reaching the hypothalamus. In turn there is no activation of the hypothalamo-pituitary-adrenal axis.

Dr. Manorama Singh[3] in 2003 in her review article explained the various ill effects of stress response. In cardiovascular system there is an increase in heart rate, cardiac output, blood pressure and increased cardiac work load. With regards to respiratory system there is an increase in respiratory rate. In circulation there is peripheral and splanchnic vasoconstriction with cerebral and cardiac vasodilatation. Metabolic changes include substrate migration with hyperglycemia, sodium and water retention. There is also immunosuppression and hypercoagulability. These changes are well tolerated by ASA 1 and 2 patients and the changes normalize with due course of time. But in patients with coronary heart disease, hypertension, diabetes, valvular heart disease (ASA 3 , 4 and 5) etc, these changes may be even life threatening.

In 2004 Deborah Burton, Grainne Nicholson, and George Hall[8] also explained the metabolic, hormonal and immunological changes associated with surgery. There is activation of the hypothalamo-pituitary axis and sympathetic system by the afferents from the site of surgery.

Overall there is increased release of catabolic hormones like cortisol, nor epinephrine and growth hormone .There is inhibition of the normal negative feedback mechanism namely, that the increased cortisol level fails to suppress the ACTH secretion from the pituitary.. On the other hand there is decreased release of anabolic hormones eg. Insulin and testosterone.

Admir Hadzic et al[9] in 2004 did a study comparing infra clavicular brachial plexus block with general anesthesia for upper limb surgeries. 52 patients were enrolled in the study, the patients were equally divided into two groups infraclavicular brachial plexus (INB) group and general anesthesia group (GA). It was seen that there was lesser post operative pain, lesser nausea, lesser vomiting, lesser incidence of sore throat and early ambulation in infraclavicular brachial plexus group when compared to general anesthesia group. It was concluded that infra clavicular brachial plexus block was better than general anesthesia with regards to post operative pain relief, early ambulation, lesser hospital stay.

In 2005 S. C. O'Riain[10] et al did a study "Inhibition of the Stress Response to Breast Cancer Surgery by Regional Anesthesia and Analgesia Does Not Affect Vascular Endothelial Growth Factor and

Prostaglandin E2". Thirty patients undergoing modified radical mastectomy were divided into two groups paravertebral anesthesia and analgesia (PVAA) group and general anesthesia with post operative opioid analgesia (GA) group. Blood samples were drawn pre operatively, 4-6 hrs and 24 hrs later. Samples were analyzed for cortisol, blood sugar, C reactive protein, vascular endothelial growth factor (VEGF) and prostaglandin E2 (PGE2). The serum cortisol and blood sugar values were significantly lower in the PVAA group at 4-6 hr when compared to the GA group. At 24 hours serum cortisol and blood sugar in both the groups were comparable. With regards to VEGF and PGE2 no significant difference was seen between both the groups at all the time intervals

Unase Buyukkocak et al[(11)] in 2005 in their study compared the effects of spinal anesthesia and general anesthesia in patients undergoing haemorrhoidectomy. Blood samples were taken pre operatively and 24 hours post operatively. Samples were sent for the analysis of IL-6, TNF-α, CRP, cortisol, and leptin. There was a post operative decrease in cortisol values but the difference was not significant. It was concluded that the difference in anesthetic technique has no influence upon the pro inflammatory and acute phase reactants in patients undergoing haemorrhoidectomy.

Unase Buyukkocak et al[12] in 2006 did a study comparing leptin, cortisol and C reactive protein in anorectal surgeries between patients administered general anesthesia vs patients given spinal anesthesia. 58 patients were included in the study. They were divided into two groups general anesthesia (ITGA) group and saddle block group. Blood samples were taken pre operatively, 3 hours and 24 hours later and was sent for cortisol, leptin and C reactive protein. There was significantly lesser cortisol levels in saddle block group when compared to general anesthesia group. It was concluded that saddle block produced lesser stress response by blocking the afferent impulses from the site of surgery.

M. Huiku et al[13] in 2007 did a study "Assessment of surgical stress during general anesthesia". Suppression of pain from the surgical site may reduce the stress response associated with surgery. In this study a surgical stress index (SSI) was computed from heart beat interval (HBInorm) and plethysmographic pulse wave amplitude (PPGAnorm). SSI was equal to 100–(0.7*PPGAnorm + 0.3*HBInorm). In this study SSI increased during skin incision and remained high throughout the procedure. SSI decrease was seen with remifentanil injections.

Katarina sakic, Marijana zura, Livija sakic, Vilena vrbanovic, Dinko bagatin [14] in 2009 analyzed the neuroimmunomodulation following general anesthesia and regional anesthesia in surgeries for cancer patients. Regional anesthesia with lesser stress response is associated with lesser immune suppression. In addition to surgical stress, hypothermia, blood transfusion, postoperative pain, and anesthetic agents themselves cause suppression of humoral and cellular immunity. Regional anesthesia improves postoperative outcome and it particularly lessens the chances of infection by attenuating perioperative immunosuppression associated with stress response to surgery.

Lakesh Kumar Anand MD, Rohit Jindal MS[15] in 2009 in Pb journal of orthopedics explained that brachial plexus block is an excellent option for upper limb surgeries. It can be given 1st preference over general anesthesia because of its various benefits. These include excellent intraoperative pain relief, decreased stress response, minimal systemic involvement, lower incidence of post operative nausea and vomiting, good post operative pain control, early ambulation and lesser hospital costs and stay.

FarheenMirza and Anthony R. Brown[16] in the year 2011 in Anesthesiology Research and Practice discussed the advantages of ultrasound guided regional anesthesia vs general anesthesia for upper limb procedures. Upper limb surgeries can be performed by general anesthesia, brachial plexus block or a combination of both. In the past general anesthesia was mostly used because of less training in blocks, increased risk of complications with brachial plexus blocks and also because of the fact that all the anesthetists are well versed with general anesthesia. However with the advent of ultra sound there is an increased interest in brachial plexus block because of lesser incidence of failures and complications. Brachial plexus block has several advantages over general anesthesia which include intra operative analgesia, post operative analgesia, good hemodynamic stability, reduced stay in PACU, better patient acceptability, and reduced incidence of post operative nausea and vomiting. With the availability of ultrasound there has been a decrease in number of block failures and complications. In conclusion ultrasound guided blocks in experienced hands has several advantages over general anesthesia and also there is a reduced incidence of complications.

At Aggo, S Fyneface-Ogan, CN Mato [4] in 2011 did study comparing the cortisol levels in patients undergoing elective lower abdominal surgeries between patients administered isoflurane based endo tracheal general anesthesia with bupivacaine based epidural anesthesia. There were 21 patients in each group. Blood samples were taken preoperatively, 30 minutes after skin incision and at the time of skin closure. The samples were sent for the analysis of cortisol. the baseline mean plasma cortisol level were 88.70 ± 3.85 ng/ml for group A and 85.55 ± 2.29 ng/ml for group B with P=0.148 showing no significant difference. At 30 minutes after skin incision the plasma cortisol level was 361.60 ± 31.27 ng/ml in GA group while it was 147.45 ± 22.36 ng/ml in the EA group, with a significant P value of 0.001. At skin closure the mean plasma cortisol value was 384.65 ± 48.04 ng/ml in the GA group which was significantly higher than the value of 140.20 ± 10.74 ng/ml in the GA group, with P<0.002. It was also found out that the blood loss was lesser in EA group when compared to the GA group. It was finally concluded that serum cortisol level was lesser in epidural group than in the GA group due to less activation of the stress response.

Mohamad H. Hamada[17] in 2012 did a study comparing cervical epidural anesthesia and interscalene brachial plexus block in patients undergoing elective upper limb surgeries. According to him nowadays regional anesthesia was preferred to general anesthesia for upper limb surgeries due to increased post operative pain relief, lesser stress response, decreased incidence of post operative nausea and vomiting. In this study patients were divided into two groups. One group received cervical epidural anesthesia while the second group surgery was done under interscalene brachial plexus block using a peripheral nerve stimulator. It was concluded that cervical epidural as well as interscalene block both were accepted anesthesia techniques. The postoperative pain relief was statistically more in group cervical epidural (33.00±5.33) than in group interscalene block(24.00± 0.00) ($p<0.005$).

Wafaa G. Ahmed and Nuha Hamdi[18] in 2012 did a study comparing the effects of different anesthetic techniques upon the cytokines and T lymphocyte subsets in patients undergoing lower abdominal surgeries. Patients undergoing lower abdominal surgeries were divided into three groups Epidural anesthesia group (EA), Total intra venous anesthesia group (TIVA) and sevoflurane based general

anesthesia group. Venous samples were taken pre induction, 2 hours later and finally 24 hours later. Samples were sent for the analysis of interleukin-6 (IL-6), tumor necrosis factor –[alpha] (TNF-_), IL-10 and cellular elements (T-lymphocyte subgroups CD4, CD8 and natural killer cells. The raise in IL-6 and TNF α at 2 hours was significantly less in epidural group when compared to TIVA and sevoflurane group. IL-10 raise at 2 hours was significant in epidural group when compared to TIVA and sevoflurane group. The decrease in CD4/CD8 ratio was less in epidural group when compared to TIVA and Sevoflurane group. The cyotokines include pro inflammatory cytokines (IL-6 and TNF α) and anti inflammatory cytokines (IL10). The balance between these cytokines prevent the spread of infection from the surgical site. The impairment of immune functions after surgery has been linked with post operative infections and even the progression of cancer. These changes in immune system following surgery may not affect the healthy people but in high risk patients they might promote cardio vascular complications, increase the risk of cancer recurrence and cause increased risk of infections. All the volatile anesthetics and opioids used in general anesthesia have immune suppression properties. In contrast in regional anesthesia the immune functions are preserved due to less activation of the stress response.

Hossein Alimohammadi, Mohammad-Reza Azizi, Saeed Safari, Afshin Amini1, Hamid Kariman, and Hamid Reza Hatamabadi [19] in 2013did a study comparing axillary nerve block versus intravenous midazolam and fentanyl analgesia for reduction of upper limb fractures. They compared the onset of anesthesia, time of recovery and post operative pain relief. The onset of anesthesia was faster in the midazolam fentanyl group. Recovery was rapid in the axillary nerve block group. Post operative analgesia was more in axillary nerve block group. From the study they concluded that though the onset of anesthesia was delayed in axillary nerve block group the recovery time and post operative analgesia was better in axillary nerve block group than the midazolam fentanyl group. The axillary nerve block based anesthesia is better than midazolm and fentanyl based anesthesia for upper limb fracture reductions.

In 2013 K Kahveci et al[20] in their study compared the stress hormone levels in patients undergoing lower limb orthopedic surgery between patients administered general anesthesia and patients administered epidural anesthesia. Totally 60 patients were included in the study. They were divided into two groups, Epidural anesthesia group (EA) and general anesthesia group (GA). Venous samples were drawn

pre operatively, then at 30 min and 24 hours after skin incision. The venous samples were sent for analysis of C reactive protein, TSH, blood sugar and cortisol levels. At 30 mins after skin incision the cortisol levels were significantly lower in EA group when compared to GA group. Also the blood sugar values were significantly lower in the EA group when compared to GA group at 30 mins.

In 2014 Marek Sadowski, Bernadeta Tułaza, Lidia Łysenko [(21)] in their review article discussed the various aspects of supraclavicular brachial plexus block. Supraclavicular brachial plexus block can be used as a sole anesthetic technique for the anesthesia for upper limb surgeries. In the past this method was not popular because of the potential side effects associated with the blind technique which include pneumathorax, phrenic nerve palsy , Horner syndrome etc. However with the recent usage of ultrasound there has been a drastic decrease of these side effects due to the accurate placement of the local anesthetic mixture near to the plexus. This has also resulted in usage of lesser dose of local anesthetic. The advantages of supraclavicular brachial plexus block include good pain control in the intra and post operative period, reduced incidence of post operative nausea and vomiting, early ambulation, good hemodynamic control and reduced surgical stress

response. In this review article they concluded that with the advent of ultrasound and with the reduced incidence of adverse effects, supraclavicular brachial plexus block has emerged as the anesthetic technique of choice for upper limb surgeries

Mathias Opperer, Thomas Danninger, Ottokar Stundner, Stavros G Memtsoudis [(22)] in 2014 in their review article explained the various benefits of spinal/ epidural anesthesia over general anesthesia in patients undergoing hip arthroplasty surgeries. Out of all the cases coming for hip arthroplasty surgeries, the percentage of patients receiving regional anesthesia is less. Regional anesthesia has the benefits of reduced blood loss, decreased incidence of thromboembolic events, reduced hospital stay and decreased costs for the patient. Another important factor is that the incidence of post operative infections are less in regional anesthesia due to reduced stress response and the immunological effects of local anesthetics and regional anesthesia.

Fereshteh Amiri, Ali Ghomeishi ; Seyed Mohammad Mehdi Aslani ; Sholeh Nesioonpour ; Sara Adarvishi[(23)] in 2014 in their study compared the stress response between spinal anesthesia and general anesthesia in patients undergoing fractional curettage. The patients were divided in two groups, one group under spinal anesthesia and the other

under general anesthesia. Venous samples were taken at 10 minutes before induction, then 20 and 60 minutes after induction. Heart rate, blood pressure were monitored every ten minutes. No significance was found out in the blood sugar levels, heart rate and blood pressure between the two groups. Thus it was concluded that there was no significant difference in terms of stress response between the two groups. One limitation in this study is that hormonal indicators of stress response were not evaluated.

Writuparna Das, Susmita Bhattacharya, Sarmila Ghosh, Swarnamukul Saha, Suchismita Mallik, Saswati Pal[(24)] in 2015 did a study comparing the effects of general anesthesia and spinal anesthesia in decreasing the stress response in patients undergoing laparoscopic cholecystectomy. A total of 30 patients were included in the study, they were divided into two groups of 15 each. Group A under general anesthesia and Group B under spinal anesthesia. In Group B patients were given spinal anesthesia in L2-L3 space with 0.5% hyperbaric bupivacaine and 25 mcg fentanyl using 26 gauge spinal needle. Then 15° Trendelenburg position was given for 10 min and sensory level was checked at intervals of 30 seconds till it reached T4 level or till 10 min, whichever comes first. Venous sample for cortisol was collected before

induction and 30 minutes after creating pneumoperitonium. The serum cortisol levels were significantly lower in the group B at 30 minutes after pneumoperitonium when compared to group A. It was concluded that spinal anesthesia for laproscopic cholecystectomy produced a significant decrease in stress response.

Stress Response and Surgery

STRESS RESPONSE

Surgery, trauma or any injury is associated with a stress response which includes a wide variety of hormonal, immunological and hematological response. The magnitude of stress response depends upon the extent and type of surgery or injury. The type of anesthesia (i.e. general or regional anesthesia), as well as the type of anesthetic agent used also have an influence upon the various hormonal and immunological changes that take place in response to stress.[1][2]

Stress response to surgery

Sympathetic nervous system activation

Endocrine ‘ stress response’

- Pituitary hormone secretion
- Insulin resistance

Immunological and hematological changes

- Cytokine production
- Acute phase reaction
- Neutrophil leukocytosis
- Lymphocyte proliferation

Ill-effects Of Stress Response:[3]

- Increase in cardiac output due to splanchnic and peripheral vasoconstriction. Also there is vasodilatation of the cerebral and coronary vessels
- Increases the heart rate, blood pressure and myocardial contractility all leading to increased myocardial oxygen demand
- Increase in respiratory rate
- Retention of sodium and water leading to reduced urine output
- Immunosuppression leading to increased chance of infections
- Protein break down leading to weight loss
- Coagulation problems like Hypercoagubility and fibrinolysis

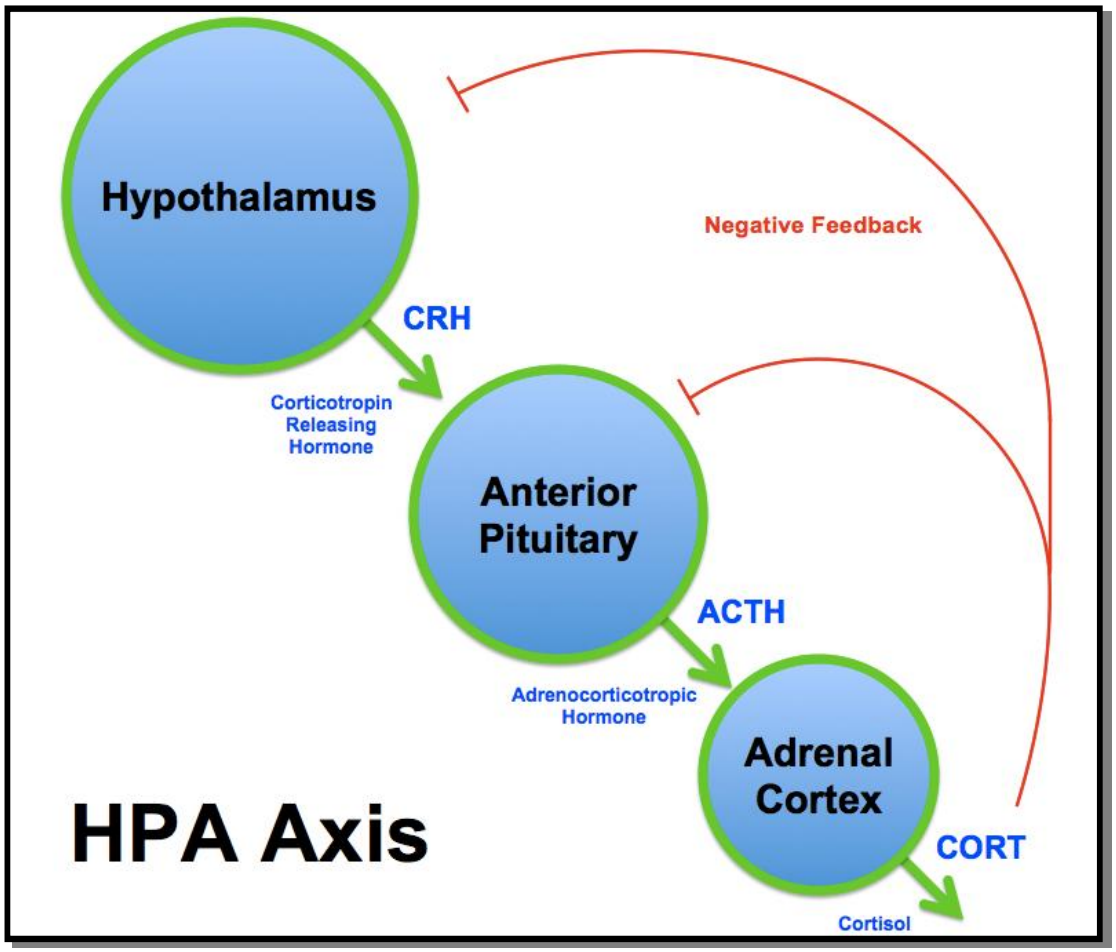
Neuroendocrine axis:

There is an increase in counter regulatory hormones or anti insulin hormones i.e. cortisol, nor epinephrine, glucagon, growth hormone. All these hormones cause hyperglycemia. The level of insulin on the other hand is normal or mildly increased. The exact mechanism of this response is not known correctly. One proposed mechanism is that the response is a neurally mediated one. Afferent impulses from the site of injury or surgery reach the hypothalamus and cause the release of various hypothalamic factors (corticotrophin releasing factor, vaso active intestinal polypeptide) which in turn stimulate the pituitary causing the release of cortisol, growth hormone, prolactin and vasopressin.

The hypothalamus also activates the sympathetic system leading to increased secretion of epinephrine from the adrenal medulla and nor epinephrine spill from the pre synaptic terminals.

Endocrine organ	Hormone	Change during surgery
Anterior pituitary	GH	Raised
	ACTH	Raised
	FSH and LH	No change
	TSH	No change
Posterior pituitary	ADH	Raised
Adrenal cortex	Cortisol	Raised
	Aldosterone	Raised
Pancreas	Insulin	Often decreases
	Glucagon	Slightly raised
Thyroid	T3, T4	Reduced [(1)]

HYPOTHALAMO PITUITARY ADRENAL AXIS



Anterior Pituitary:

Stimulation of anterior pituitary by hypothalamic releasing factors cause the release of Adreno Cotrtico Tropic hormone (ACTH), growth hormone and prolactin. The concentration of other hormones i.e. Thyroid stimulating hormone (TSH), Follicle stimulating hormone (FSH), Luteinizing hormone (LH) do not change significantly

Posterior pituitary :

Increased levels of anti diuretic hormone are produced.

CORTISOL:

It is a steroid hormone which is produced from the adrenal cortex in response to stimulation from ACTH produced from anterior pituitary. It is a glucocorticoid also known as hydrocortisone.

The secretion of cortisol from the adrenal cortex decreases as the day goes by with the maximum levels seen 6- 8 AM and the lowest at around midnight. The peak value is around 23 mcg/dl. Around 20 mg is produced per day but the levels may raise up to 150 – 300 mg /day.

Increased levels of cortisol are seen following surgery or injury due to increased stimulation by elevated levels of ACTH. During surgery the cortisol levels may increase from a baseline value of about 400 nmol/litre to reach a maximium of about 1500 nmol/ litre at 4 to 6 hour depending upon the severity of injury and surgery. This response to surgery is decreased in adrenelectomized animals and patients with Addison's disease[(8)].

Usually there exists a negative feedback mechanism i.e. increased cortisol levels act on the hypothalamus and decrease the release of

corticotrophin releasing hormone. But this mechanism seem to be blunted during surgery as the level of both ACTH and Cortisol is increased.(1)

Actions of cortisol:

- Promotes glycogenolysis
- Promotes gluconeogenesis
- Decreases peripheral glucose utilization
- Increases insulin resistance

} increases blood glucose

- Causes lipolysis
- Causes proteolysis
- Anti inflammatory property- interfere with the accumulation of neutrophils , macrophages and also interfere with the synthesis of inflammatory mediators especially prostaglandins

Metabolic sequelae to endocrine response:

The overall effect of endocrine response to surgery include increased secretion of catabolic hormones. These hormones provide food substrate from the breakdown of carbohydrate, fat and protein. In current anesthesia practice these effects have a detrimental effect on the patient outcome.

Carbohydrate metabolism:

Increased levels of cortisol, cathecolamines and glucagon lead to increased glucose level in the blood by increasing the glycogenolysis, and gluconeogenesis in liver. The blood glucose concentrations in turn depend upon the intensity of surgical stimulus. The usual mechanisms maintaining the glucose hemostasis in the perioperavtive period are affected, due to increased levels of catabolic hormones and increase in insulin resistance which ultimately lead to hyperglycemia.

Prolonged perioperative hyperglycemia is associated with wound infection and poor wound healing in the perioperative period. An increased incidence of wound infection was found with diabetics and non diabetics with sugar levels greater than 250mg/dl[(1)]

Fat metabolism:

The hormonal changes cause lipolysis of triglycerides to glycerol and fatty acid. This lipolysis is promoted by cortisol, cathecolamines and glucagon. The lipolysis is inhibited by insulin. The glycerol so produced is used as a substrate for glucose production in the liver by gluconeogenesis. Ketone body production may also be increased

Protein metabolism:

Cortisol, glucagon and cathecolamines increase the breakdown of proteins into amino acids. This protein breakdown occurs in both injured tissue as well as in uninjured skeletal muscle. These amino acids are then transported to liver for glucose production (gluconeogenesis) and protein synthesis. The hepatic protein synthesis of acute phase proteins (i.e. C-reactive protein, alpha 1 acid glycoprotein, alpha 1 antitrypsin, ceruloplasmin, etc.) increases. The degree of acute phase response increases proportional to the tissue injury. Protein catabolism leads to marked weight loss and muscle wasting in patients after major surgeries.

Water and electrolyte metabolism:

Increased secretion of anti diuretic hormone (ADH) from the posterior pituitary results in water retention and the production of a concentrated urine. These effects may continue for at least 3- 5 days depending upon the surgical injury.

Renin secretion from juxtaglomerular cells increases, leading to increase production of aldosterone. This is due to sympathetic stimulation. Aldosterone causes sodium and water reabsorption from the distal convoluted tubules of the kidney.

IMMUNOLOGICAL CONNECTION:

Cytokines:

Cytokines are a group of proteins which play a major role in mediating immunity and inflammation. They are produced from activated leucocytes, fibroblasts and endothelial cells as in response to injury. Cytokines include interleukins and interferons.

After surgery the main cytokines released include interleukin 1(IL-1), interleukin 6 (IL-6) and Tumour necrosis factor alpha (TNF-α). The initial response is the release of IL-1 and TNF α from the macrophages and monocytes in the damaged tissues. This in turn stimulates the release of other cytokines in particular IL-6 , the main cytokine responsible for inducing the acute phase response.[(2)(25)]

Interaction between immune system and neuro endocrine system:

IL-1 plays an important role in activating the response to surgical stress. IL-1, IL-2 and INF gamma stimulate ACTH secretion from the pituitary which in turn increases cortisol secretion from the adrenal cortex. A negative feedback mechanism exists whereby glucocorticoids inhibit cytokine production [(1)]. Glucocorticoids are known to cause suppression of cellular immunity. They decrease the levels of IL-1,

interferon gamma and IL-2; block phospholipase A2 which is necessary for the production of prostaglandins and leukotrines; block the action of proteases involved in inflammation.[3]

Effects of Different Anesthetic Techniques on Stress Response

THE EFFECT OF ANESTHESIA ON STRESS RESPONSE TO SURGERY

GENERAL ANESTHESIA:

Opioids:

Opioids are known to suppress hypothalamic and pituitary hormone secretions. However large doses are required to suppress the stress response. Morphine, fentanyl 50-100 mcg/ kg, sufentanil20 mcg/kg, alfentanil 1.4mg/kg have been found to suppress the pituitary hormone secretions. However these large doses of opioids invariably leads to respiratory depression after surgery, which may require prolonged post operative ventilation.[1][4]

Inhalational agents:

In general inhalational agents are not able to suppress the stress response to surgery in the normal doses that are used.[3]

Intra venous inducing agents:

Propofol and thiopentone do not suppress the stress response. Etomidate[26] on the other hand is known to suppress the secretion of adrenal steroids by reversibly inhibiting the enzyme 11 β hydroxylase.

This enzyme inhibition may last for 4- 8 hrs after the induction dose of etomidate. When used as a continuous infusion in critically ill patients, it is associated with increased mortality.

Benzodiazepines like midazolam and diazepam are seen to reduce the cortisol secretion in response to surgery. But large doses may be required which are associated with side effects.[1]

α 2 agonists:

Clonidine and dexmedetomidine are centrally acting α 2 agonists. These drugs by acting on the pre synaptic α 2 receptors, decrease the sympathetic outflow, thereby reducing the stress response to surgery.

REGIONAL ANESTHESIA:

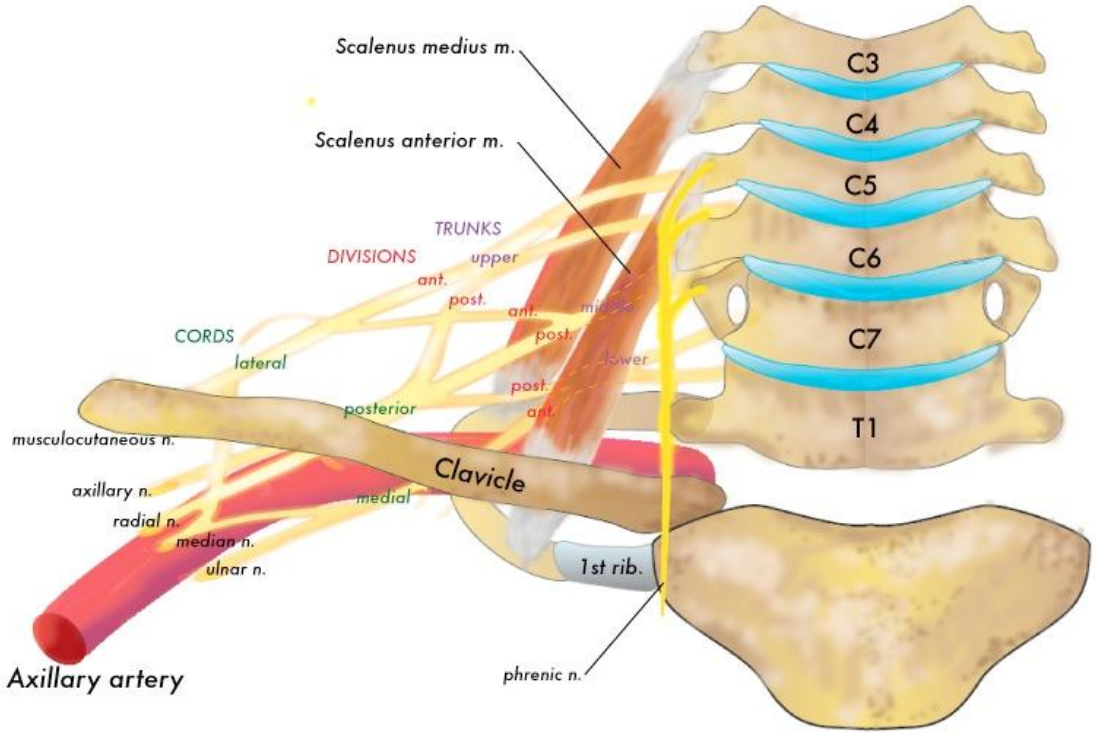
In regional anesthesia there is complete blockade of nerve supply to the surgical field[1][8]. The afferent stimulus from the surgical site do not reach the central nervous system, so in turn there is no activation of hypothalamus leading to lesser stress response. In epidural analgesia there is also blockade of the efferent autonomic neural pathway to the liver and the adrenal medulla. Thus overall the adrenocortical and the glycemic response to surgery is blocked(4). In inadequate blockade the stress response may not be completely blocked because some afferents

may reach the central nervous system and cause stimulation of the hypothalamo-pituitary-adrenal axis. Regional anesthesia has advantages over general anesthesia with regards to better intra operative pain control, post operative analgesia[15], reduced incidence of post operative nausea and vomiting[27], as well as reduced hospital stay.

SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK:

It is often called “the spinal anesthesia of the upper extremity” because of its unique application to the upper extremity block. The first percutaneous block was performed by Kulenkampff in Germany in 1911. A few months later, axillary approach of brachial plexus block was described by Hirschel. Kullenkampff and Persk in 1928 published their experience with thousand blocks without any apparent complications.

The block is performed at the level of the distal trunks and origin of divisions, the place at which the brachial plexus is confined to a small area. The three trunks carry the sensory, motor and autonomic fibres to the entire upper limb except a small area on the medial aspect of the arm.



Land marks:

An important anatomical landmark in supraclavicular block is the identification of the subclavian artery. The subclavian artery lies in front of the lower trunk of the brachial plexus and its branches.

The sternocleidomastoid muscle inserts on the medial third of the clavicle, the trapezius on the lateral third of the clavicle and the neuromuscular bundle passes through the middle third of the clavicle. During supraclavicular brachial plexus block there are more chances of puncturing the pleura either at the pleural dome (more likely) or through the first intercostal space. A good knowledge about the anatomical position of the pleura is very important in supraclavicular block in order to reduce the chances of pneumothorax. Within the cavity of the 1st rib the pleural dome is contained. Because the first rib crosses under the junction of the medial and the middle third of the clavicle its path coincides with the insertion of the sternocleido mastoid muscle, which inserts on the middle third of the clavicle. Thus the lateral insertion of

the sternocleidomastoid muscle on the clavicle can be used as a land mark for the location of the 1st rib and of the lateral edge of the dome of diaphragm.

INDICATIONS:

Supraclavicular block can be used for the surgeries of upper limb distal to the shoulder, including the upper arm and elbow as well as forearm, wrist and hand.

Approaches to supraclavicular block:

1. Classical approach of Kulenkampff
2. Perivascular approach of Winnie and Collins
3. Modified lateral paravascular approach of Moorthy.

For the supraclavicular block the patient should be positioned supine, with the head turned to the opposite side

Classical approach:

The neede entry point is just 1 cm above the clavicle in the mid clavicular line, just lateral to the subclavian artery pulsation. The needle is then directed posteriorly, medially and caudally until the brachial plexus is reached.

Complications:

- Pneumothorax
- Horner syndrome
- Phrenic nerve palsy
- Accidental intravenous injection of local anesthetic

Pharmacology

PHARMACOLOGY

LOCAL ANESTHETICS:[28]

- They are used to provide analgesia and anesthesia
- They produce reversible blockade of conduction of impulses along the central as well as peripheral nerves
- They act by blocking the sodium channels
- Thus they prevent the propagation of action potential along the nerves
- All local anesthetics are weak bases. Their pKa values are higher than physiological pH.

Classification

AMIDES	ESTERS
Lignocaine	Cocaine
Bupivacaine	Procaine
Etidocaine	Bezocaine
Levobupivacaine	Tetracaine
Mepivacaine	Chlorprocaine
Prilocaine	
Ropivacaine	

LIGNOCAINE:

Pka	Protein binding	Vd (litres)	T1/2 (mins)	Clearance (litres/min)	Onset	Duration (mins)
7.9	70	91	96	0.95	Rapid	60-120

Metabolism:

- Mainly metabolized in the liver by oxidative dealkylation
- Hepatic disease or decrease in hepatic blood flow that may occur with anesthesia may decrease the metabolism of lignocaine

Clinical uses:

- Topical – 4%
- Infiltration- 0.5-1%
- Intra venous regional anesthesia 0.25-0.5%
- Peripheral nerve block- 1-1.5%
- Epidural- 1.5-2%
- Spinal- 2-4%

Dosage:

4 mg/ kg

7 mg/kg with1 in 200000 adrenaline

Side effects:

Plasma lignocaine concentration (mcg/dl)	**Effect**
1-5	Analgesia
5-10	Tinnitus, circumoral numbness, skeletal muscle twitching, systemic hypotension
10-15	Seizures, unconsciousness
15-25	Coma, apnoea
>25	Cardiovascular depression

BUPIVACAINE:

Pka	**Protein binding**	**Vd (litres)**	**T1/2 (mins)**	**Clearance (litres/min)**	**Onset**	**Duration (mins)**
8.1	95	73	210	0.47	Slow	240-480

Metabolism:

- Mainly metabolized in the liver
- Small percentage is eliminated unchanged in the urine
- Alpha 1 acid glycoprotein is the most important binding site of bupivacaine.

Dosage:

2.5 mg/kg

Uses:

- Infiltration 0.25%
- Peripheral nerve block- 0.25- 0.5%
- Epidural- 0.5-0.75%
- Spinal- 0.5-0.75%

SIDE EFFECTS:

Cardiovascular system

- Accidental iv injection of bupivacaine can produce severe hypotension, cardiac dysarrhythmias, and AV block
- This is due to the depression of the maximal depolarization rate of the cardiac action potential (Vmax) by its ability to inhibit sodium channels. Tachycardia can enhance toxicity

Central nervous system:

- Systemic absorption may produce central nervous system stimulation or depression or both
- Apparent central nervous system stimulation is manifested as restlessness, tremors progressing to convulsions followed by depression and coma leading to death by respiratory arrest

Treatment of Bupivacaine induced cardiotoxicity:

- 20 % lipid emulsion- 1.5ml/kg
- Continue infusion at 0.25 ml/kg/min for atleast 10 minutes after return of normal cardiac functions
- If cardiovascular instability continues, the bolus dose can be repeated and the infusion can be increased to 0.5ml/kg/min
- Maximum dose of 20% lipid emulsion is 10 ml/ kg over 30 minutes
- The intra lipid emulsion acts like a plasma sink and absorbs the tissue bound local anesthetic via partition principle

PROPOFOL:[29]

- It is a non barbiturate intravenous inducing agent
- It probably acts on the Gamma Aminobutyric acid (GABA) receptors.
- Binding of propofol to GABA A receptor causes prolongation of action of GABA and increased duration of opening of chloride channel resulting in hyperpolarisation of postsynaptic cell membrane causing functional inhibition of postsynaptic neurons

Pharmacokinetics:

PKa	Clearance (ml/Kg/min)	Vd (litres/kg)	Protein binding
11	30-60	3.5-4.5	95-98%

Dosage:

Induction dosage- 1.5- 2.5 mg/kg

Uses:

- Inducing agent
- Maintenance of anesthesia
- Treatment of laryngospasm

CONTRAINDICATIONS:

Absolute contraindications:

1. Known hypersensitivity to Propofol or any of its components.
2. Contraindicated in patients with allergies to eggs, egg products, soybeans or soy products.
3. Disorders of fat metabolism

Relative contraindications:

1. In patients undergoing stereotactic neurosurgery such as pallidotomy, as it temporarily abolishes tremors in patients with Parkinsonism.
2. Known case of Epilepsy
3. Untreated hypertensive, hypovolemic patients with impaired Left ventriclular function
4. Hepatic or Renal impairment
5. Pregnant and lactating mother

SEVOFLURANE:[30]

- Halogenated Methyl ethyl ether
- Non pungency and rapid increase in alveolar concentration makes it the ideal agent for inhalational induction in pediatric and adult population.

Physical and chemical properties:

- Molecular weight- 200
- Boiling point-58.5 degree celsius
- Vapor pressure (mmHg, 20 degree Celsius)- 170
- Odor- ethereal
- No preservative
- Blood gas partition coefficient- 0.69
- Minimum alveolar concentration- 1.80

Metabolism:

- 4% metabolized in the liver
- Metabolites are inorganic fluoride and organic hexa fluro isopropanol

EFFECTS ON ORGAN SYSTEMS:

Central nervous system

- Cerebral blood flow is increased leading to mild increase in intra cranial pressure. But the change is less pronounced than halothane. Intra cranial pressure can decrease with prior hyperventilation

- Cerebral metabolic rate is decreased

Cardiovascular system:

- Decreased myocardial contractility
- Decreased systemic vascular resistance
- Minimal or no change in heart rate

Respiratory system:

- Decrease in Tidal volume and increase in respiratory rate
- Causes respiratory depression

Toxicity:

- Only volatile agent that does not produce trifluro acetic acid as metabolite → no Hepatotoxicity

- Compound A production with dry soda lime which causes renal failure in rats but no proven renal failure in humans
- Can Trigger Malignant hyperthermia

FENTANYL:[31]

- A phenylpiperidine- derivative synthetic opioid agonist.
- As an analgesic 75-100 times more potent than morphine

Pharmacokinetics:

- iv injection produces rapid and shorter duration of action than morphine

pK	**Clearance (ml/min)**	**Protein binding**	**Vd (litres)**	**Partition coefficient**	**T1/2(hrs)**	**Context sensitive half time**
8.4	1,530	84	335	955	3.1-6.6	260

Clinical uses:

- 1-2 mcg/ kg provide analgesia
- 2-20 mcg/kg are used as an adjuvant to inhaled anesthetics to blunt the circulatory responses to laryngoscopy , sudden change in the level of surgical stimulation
- Large doses of fentanyl can be used alone to produce surgical anesthesia. They have stable hemodynamics due to lack of myocardial depressant effects, absence of histamine release and they reduce stress response to surgery

Side effects:

- Possible patient awareness
- Respiratory depression with high doses
- No decrease in stress response in low doses
- Chest wall rigidity
- Cough during rapid administration of the drug

Materials and Methods

MATERIALS AND METHODS

The study was done in the Department of Anesthesiology, ESIC MC AND PGIMSR, K. K Nagar,Chennai from September 2014 to June 2015.

STUDY DESIGN:- Prospective randomized control study.

Participants:

Patients posted for upper limb surgeries were included in the study. The protocol of the study was approved by the Institutional ethical committee of ESIC MC AND PGIMSR, K. K Nagar,Chennai. After obtaining departmental approval and written informed consent from the patients, American Society of Anesthesiologist grade I and II patients of both the sex ,between 18- 64 years scheduled for elective upper limb surgeries were included in the study.

Inclusion Criteria:

- Patients of both sex 18-60 years of age
- Planned for arm, forearm and hand surgeries
- ASA physical status I and II

Exclusion criteria:

- Patients with bleeding disorders and patients on anti coagulation medications
- Infection at the site of supraclavicular block injection
- Contra lateral lung injury or rib fractures
- Neuropathy involving the upper limb
- Allergy to local anesthetics
- Pregnant women
- Emergency surgeries

A detailed explanation regarding the study was given to the patients and a written informed consent was obtained from the participants of the study.

BASELINE EVALUATION:

The basic evaluation included

- Detailed history
- General and systemic examination
- Height , weight, body mass index, pulse rate, blood pressure and saturation were recorded

LABORATORY INVESTIGATION:

In all the patients a set of biochemical investigations were carried out as a part of routine pre anesthetic evaluation which included

- Complete haemogram
- Blood urea nitrogen
- Serum creatinine
- Random blood sugar
- Liver function tests
- Electro cardiogram
- Chest X ray

INTERVENTION:

- All patients fasted overnight
- 3ml blood sample collected 1 hour before surgery for baseline serum cortisol estimation

RANDOMIZTION

PATIENTS ARE DIVIDED INTO TWO GROUPS

BY SLIPS IN BOX TECHNIQUE

GROUP GA	GROUP RA
Under GENERAL ANAESTHESIA	Under SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK

- Patient shifted to OT in a trolley by trained person
- Standard monitors are attached
  - Pulse oximetry for saturation (SpO2) .
  - Non invasive blood pressure monitoring.(NIBP)
  - Electrocardiogram (ECG).
  - Baseline pulse rate, blood pressure, oxygen saturation are recorded.
  - An intravenous line is started and connected with RINGER LACTATE/NORMAL SALINE at 100 ml /hr.
  - Inj midazolam 1mg and inj glycopyrolate 0.2 mg iv given
  - Oxygen at the rate of 4l/min administered through face mask.

Vital parameters will be observed throughout the procedure every 15 minutes as usual and recorded.

Surgery in RA group:

A set containing following is used for the RA group:

- Insulated Stimulator needle
- Peripheral nerve stimulator
- ECG electrode
- Two 20 ml syringes
- Skin marker pencil
- One tuberculin syringe of 1 ml
- Two stainless sterile bowls one each for iodine and spirit.
- Sterile gauze pieces, one sterile swab.

TECHNIQUE **Supraclavicular block –classical approach(nerve-stimulator technique**)

1. Dorsal recumbent position without a pillow. Arms at his/her sides and head turned to side opposite to the one being blocked.

- Small pad is placed below bilateral shoulder.
- The patient is asked to lower the shoulder and flex the elbow, so that the forearm rests on his/her lap.
- The wrist is supinated so the palm of the hand faced the patient's face**.**

2. Part of neck was aseptically cleaned and draped.

3. The operator stands on the side to be blocked so for a left side block the palpation is done with the left hand and the needle is manipulated with the right and vice versa.

4. The lateral (posterior) border of the sternocleidomastoid (SCM) muscle is identified and followed distally to the point where it met the clavicle.

    - The point of needle entrance is about 1 inch (2.5 cm) lateral to the insertion of the SCM in the clavicle or one "thumb breadth" lateral to the SCM.
    - Palpation of the subclavian artery at this site confirms the landmark. The palpating index finger is placed at this site.

5. Local infiltration of 1ml of 2% lignocaine is given

6. An insulated needle will be used to perform this technique. The needle is connected to nerve locator by the electrodes and is properly grounded with the help of ECG lead.

The stimulation is started with an intensity of 2.0 mA and a pulse width of 100 μs. Once the desired response is obtained – that is a muscle twitch of the fingers that is clearly visible – the current is gradually decreased up to 0.6mA.

If the response is obtained at 0.4mA also, then the needle is repositioned again so as to get response at 0.6mA but not at 0.4mA

7. If the response was not adequate or if repositioning of the needle is necessary, the needle is withdrawn and the penetration angle is adjusted in the anteroposterior plane.

As a goal we aimed to elicit an isolated muscle twitch in all fingers either in flexion or extension.

Wrist flexion and extension of the fingers is taken as acceptable responses and the current gradually reduced between 2 to 0.5 mA. The total volume of the anesthetic solution is injected at an incremental dose of 5ml each, preceded by negative aspiration.

- 3-min massage is performed to facilitate an even drug distribution.
- Adequacy of block is checked by pin prick method for sensory blockade and by modified Bromage scale for motor block
- The surgery is allowed to proceed when complete anesthesia is achieved.
- 3ml of blood samples are taken at 30mins, 3 hrs and 24 hrs after skin incision for serum cortisol estimation

- Post operative follow up is carried out in the recovery and post operative ward. 3ml of blood sample is taken in the post operative ward at 24 hrs after skin incision

SURGERY IN GA GROUP

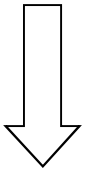
- Anesthesia was induced in supine position in all the patients in this group
- Patients were pre-oxygenated for 3 minutes with 100% oxygen at a flow rate of 8 l/min
- Intravenous fentanyl 2 mcg/ kg given
- Patients are then induced with inj propofol 2mg/ kg and then inj vecuronium 0.1mg/kg is given patients then are intubated with appropriate size endotracheal tube
- Maintenance of anesthesia with N2O and O2 at 67% and 33% respectively and sevoflurane 2%
- At the end of surgery the residual muscle relaxation is antagonized with inj neostigmine 0.05 mg/ kg and inj glycopyrolate 0.02mg/kg
- 3 ml blood samples are taken at 30 mins, 3 hours and 24 hours after skin incision for serum cortisol estimation

PATIENT FLOW CHART

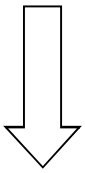
ASSESMENT CLINIC ASA I and ASAII

(18- 60 years of either Sex)

Informed consent



ON THE DAY OF SURGERY



RANDOMISATION

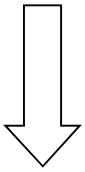
GROUP GA

GROUP RA

Pre operative blood sample

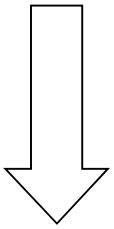
Patient shifted to the operation theatre by a trained personnel in a trolley.

INSIDE THEATRE



WHO CHECK LIST

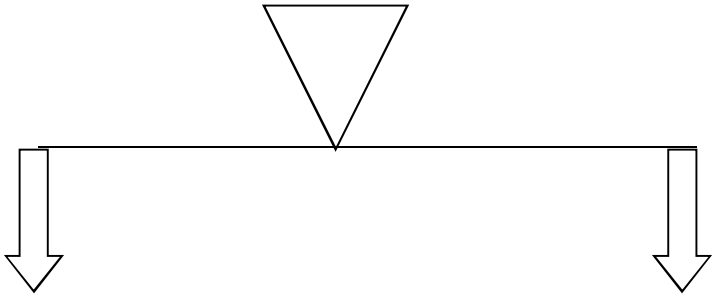
Monitors connected



Airway cart and rescue measures

Intravenous line access

Inj midazolam 1mg, inj glycopyrolate 0.2 mg



GROUP GA

Routine induction with

- **Inj Propofol 2mg/ kg**
- **Inj. Fentanyl 2mcg/ kg**
- **Inj vecuronium 0.1mg/kg**

GROUP RA

- **Bupivacaine 0.5%- 15 ml**
- **Lignocaine with adrenaline 2%- 15 ml**

Intra operative blood sample taken at

30 minutes and 3 hours of skin incision

Post-Operative Period- Blood Sample Taken At

24 Hours After Skin Incision

Statistics and Results

STATISTICAL ANALYSIS AND RESULTS

Sample size was calculated using N Master version 1.0. The total sample size was calculated to be 57. In this study a total of 62 patients were included. One patient was excluded from the study due to lysis of blood sample. The remaining patients were divided into two groups, Group GA with 30 patients under general anesthesia and Group RA with 31 patients under supraclavicular brachial plexus block.

In the above study, the data were either quantitative data or qualitative data. For quantitative data descriptive statistics was presented by Mean (N), Standard Deviation and Range. For qualitative data, frequency count (N) and percentage were displayed in a tabular manner.

For statistical analysis SPSS (version 16.0) software was used. To analyze the data appropriate statistical tests were applied such as to compare the two groups Independent Samples t-Test was used. Other data displayed by various tables and charts by using Microsoft excel (windows 2010).

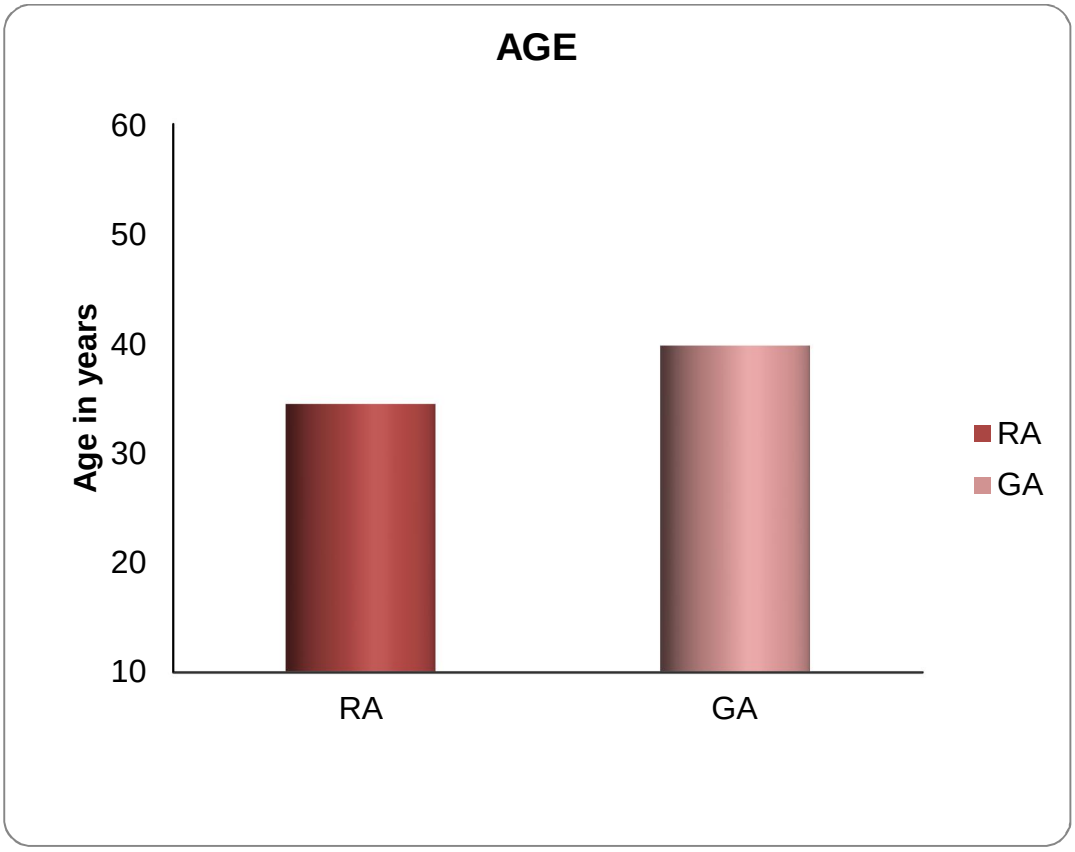
*Significant at $p < 0.05$

** very significant $p < 0.01$

*** highly significant $p < 0.001$

Table 1: Age Distribution

Group	Group RA	Group GA	P value
AGE	34.48	39.80	0.073



With regards to age distribution the two groups are comparable with each other with P value 0.073

Table 2: Sex Distribution

Group	RA	GA
MALE	26	21
FEMALE	5	9

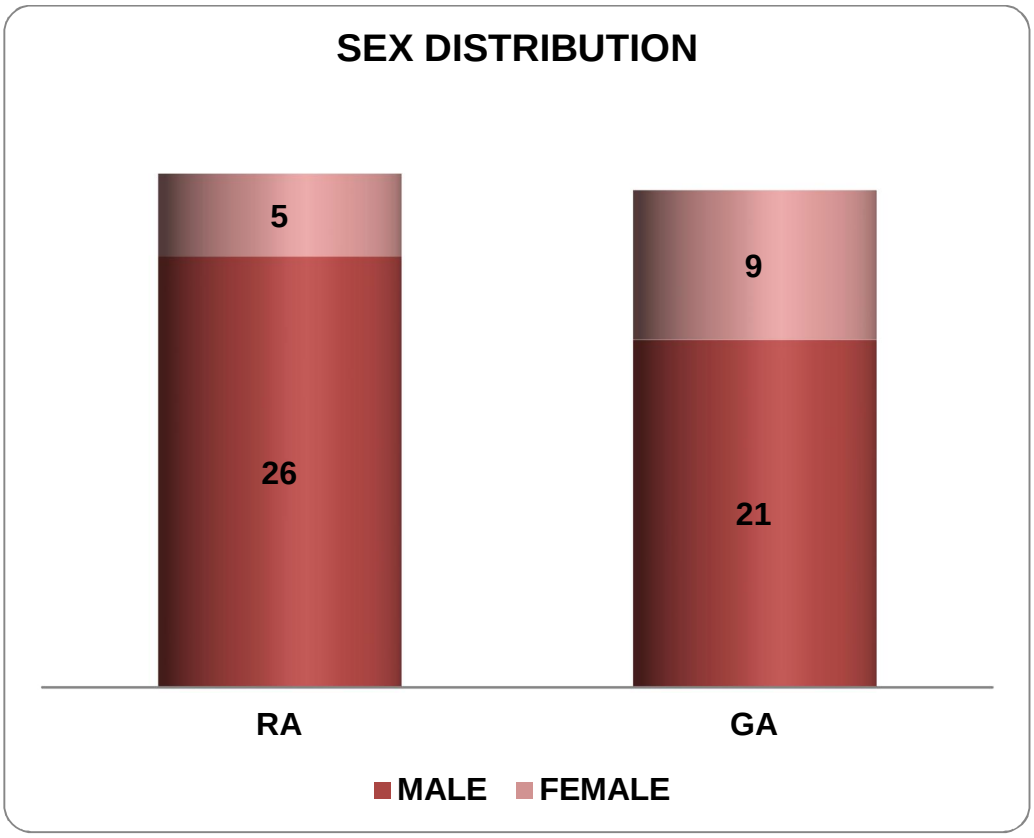


Table 3: Comparison Of ASA Class Between The Two Groups

Groups	RA	GA
ASA I	26	18
ASA II	5	12

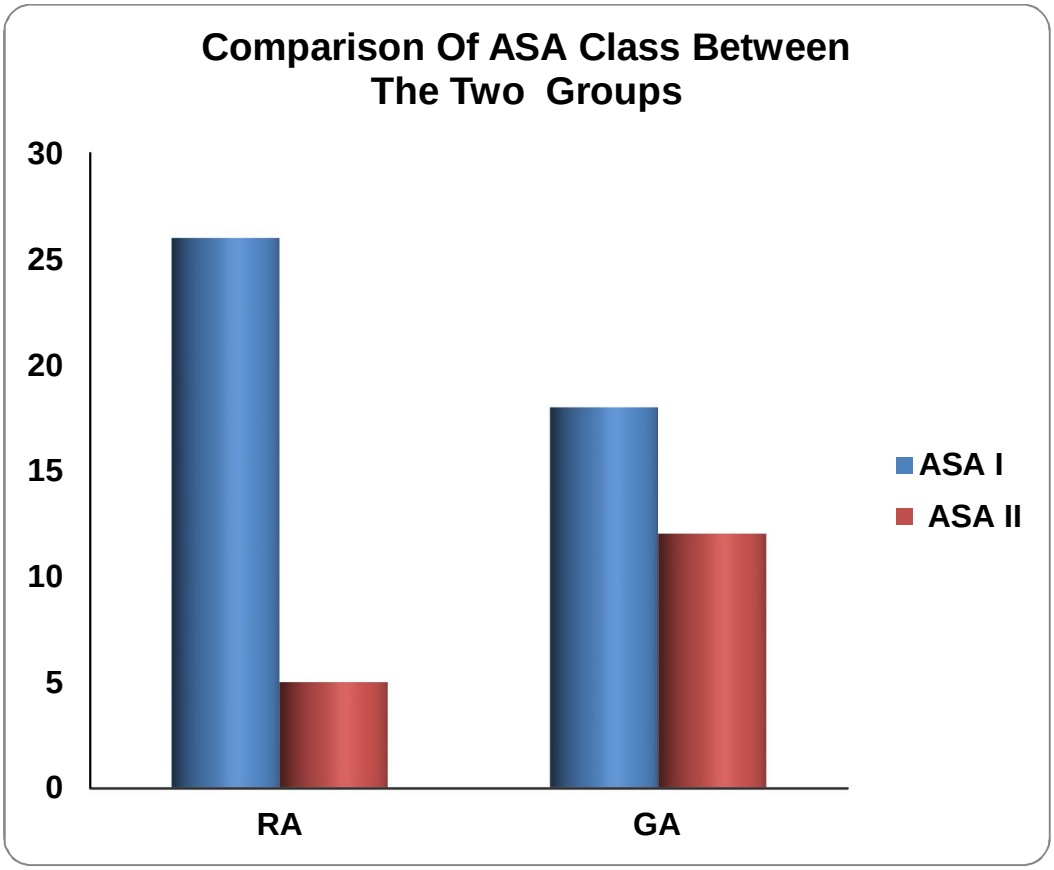
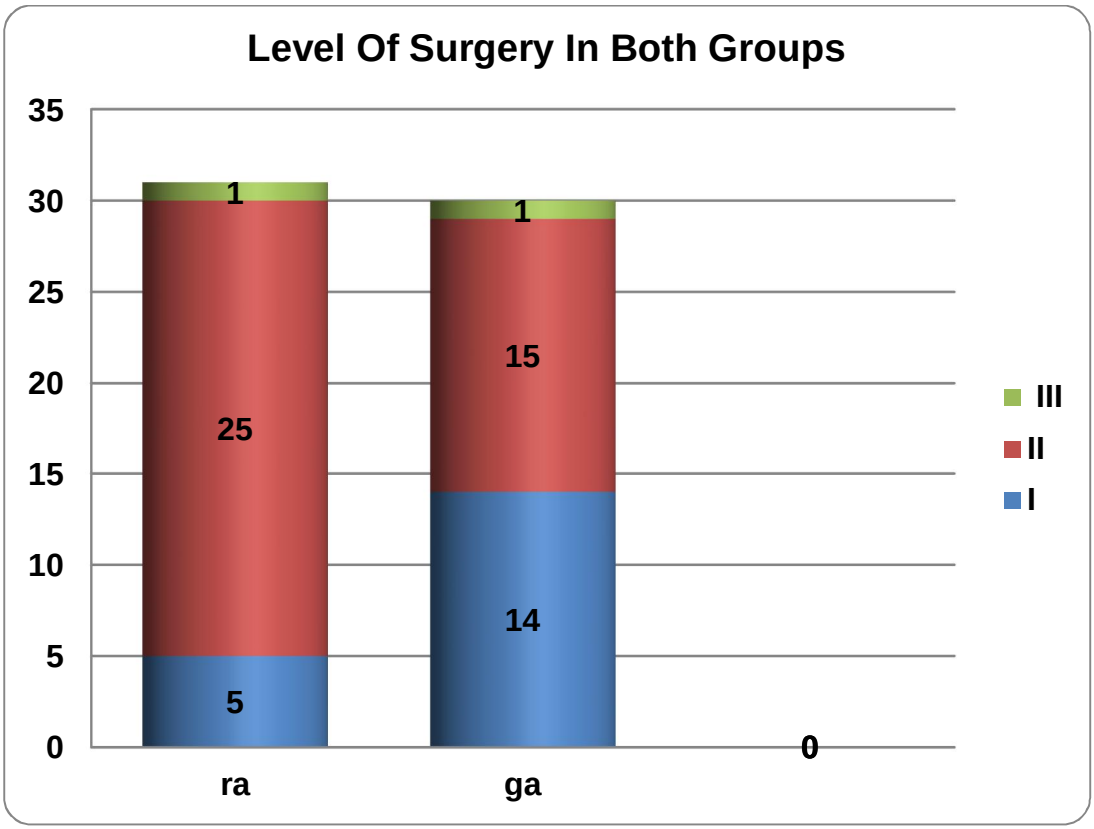


Table 4: Level Of Surgery In Both Groups

Group	RA	GA
Level I	5	14
Level II	25	15
Level III	1	1



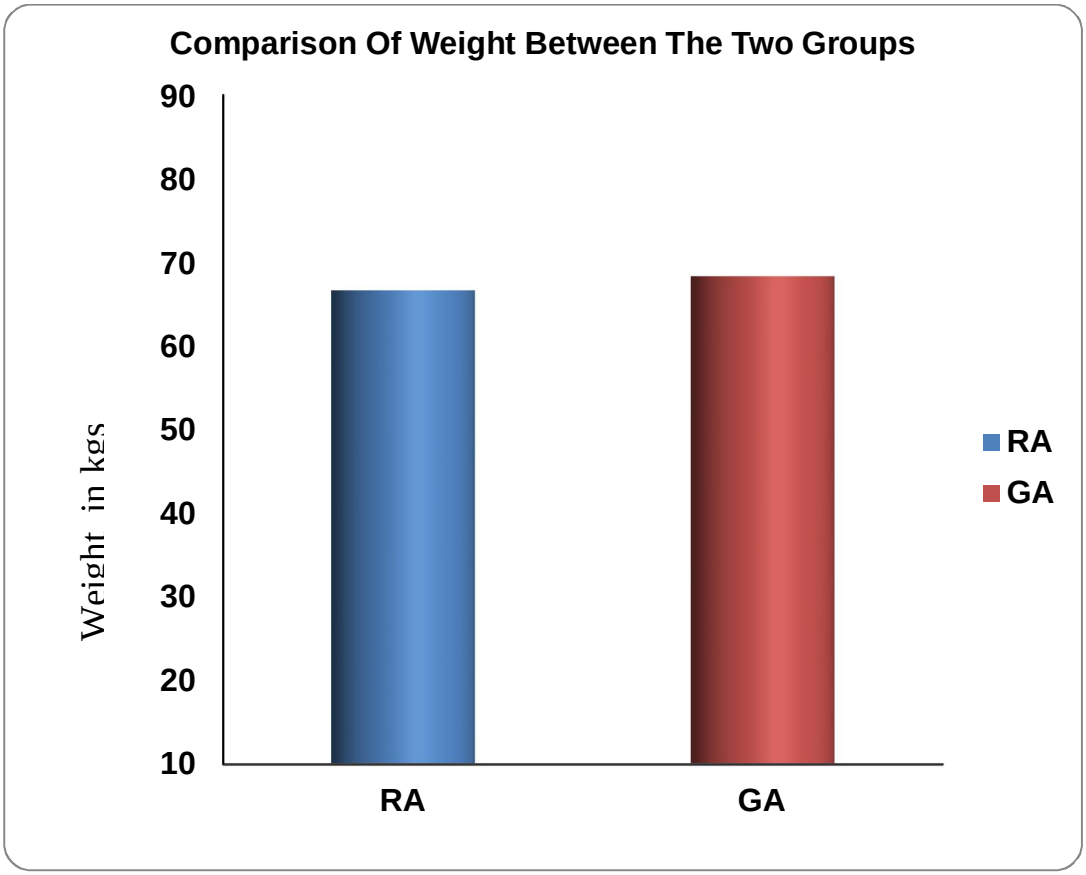
I- Elbow and above elbow surgery

II- Forearm surgery

III- Hand surgery

Table 5: Comparison Of Weight Between The Two Groups

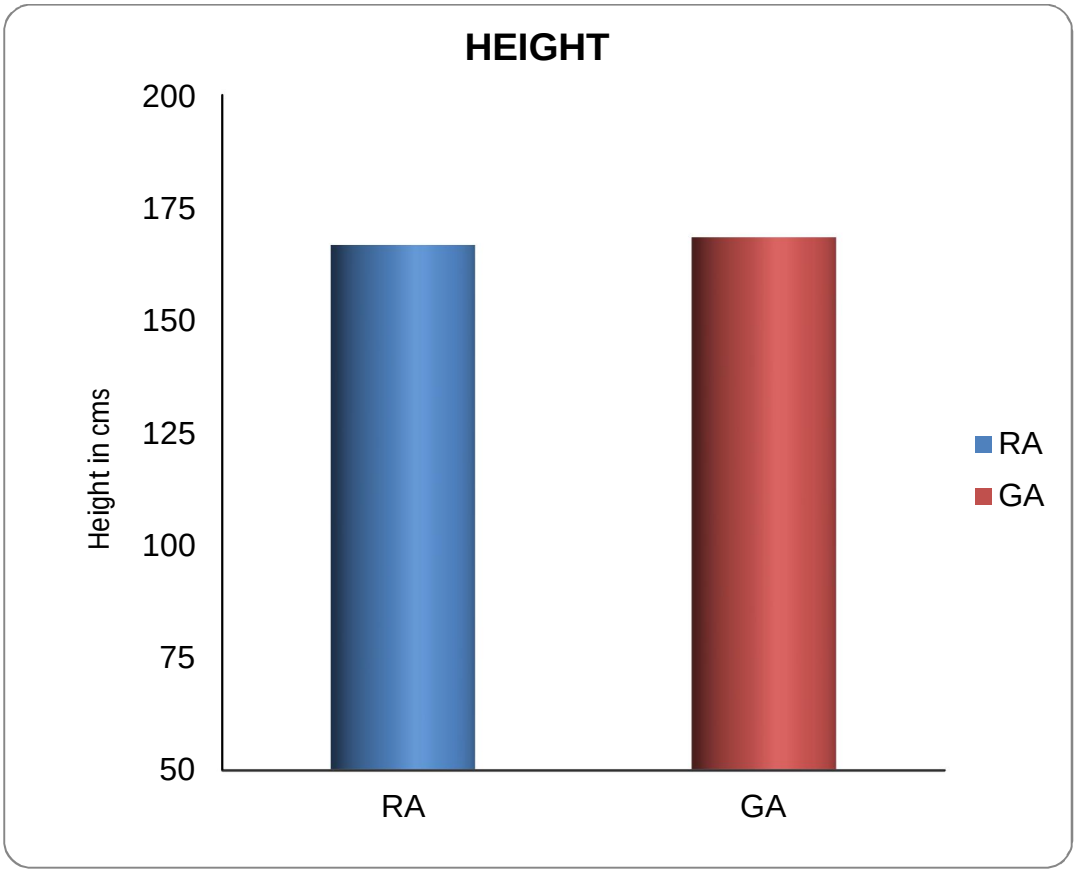
Group	RA	GA	P value
Weight in kgs	66.77	68.40	0.318



As regards to weight the two groups are comparable with each other with P value Of 0.318

Table 6: Comparison Of Height Between The Two Groups

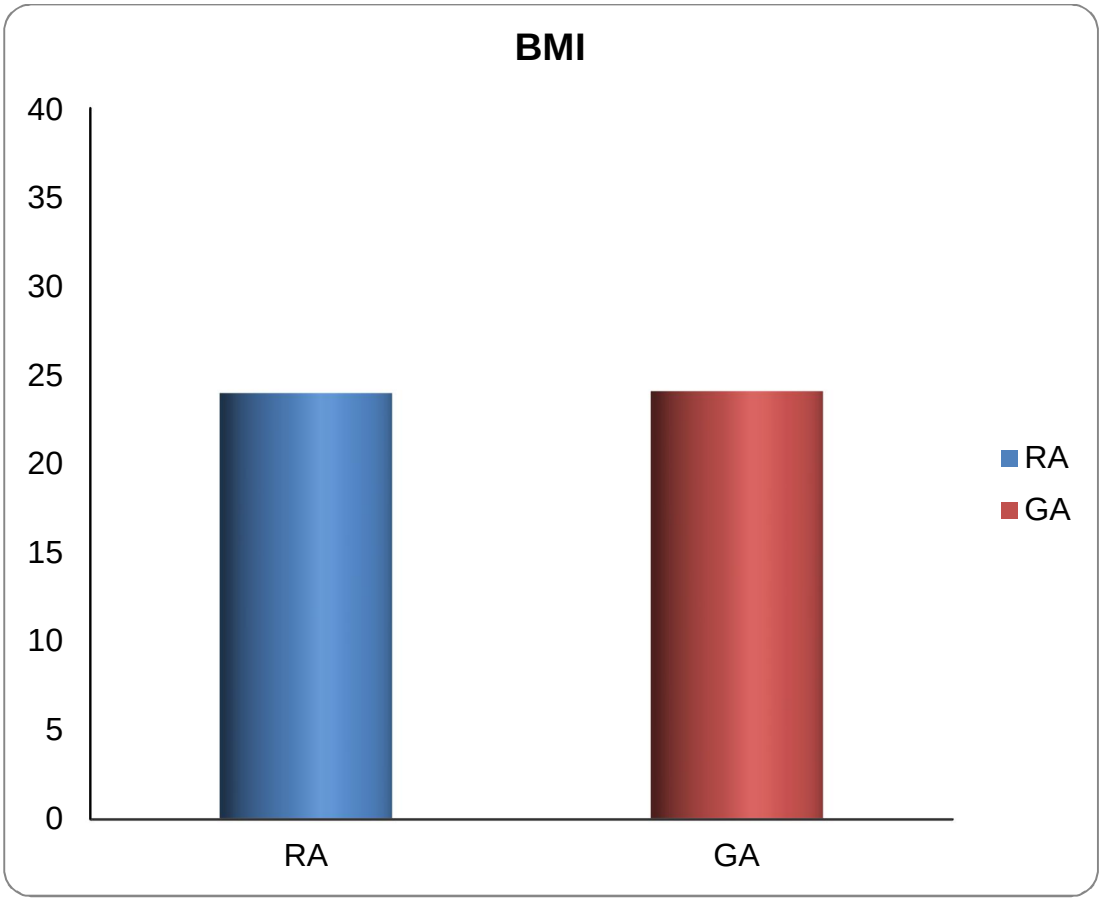
Group	RA	GA	P value
Height in cms	166.74	168.47	0.276



The height of the patients in the two groups are comparable with P value of 0.276

Table 7: Comparison Of BMI Between The Two Groups

Group	RA	GA	P value
BMI in kg/ square meter	23.98	24.09	0.782

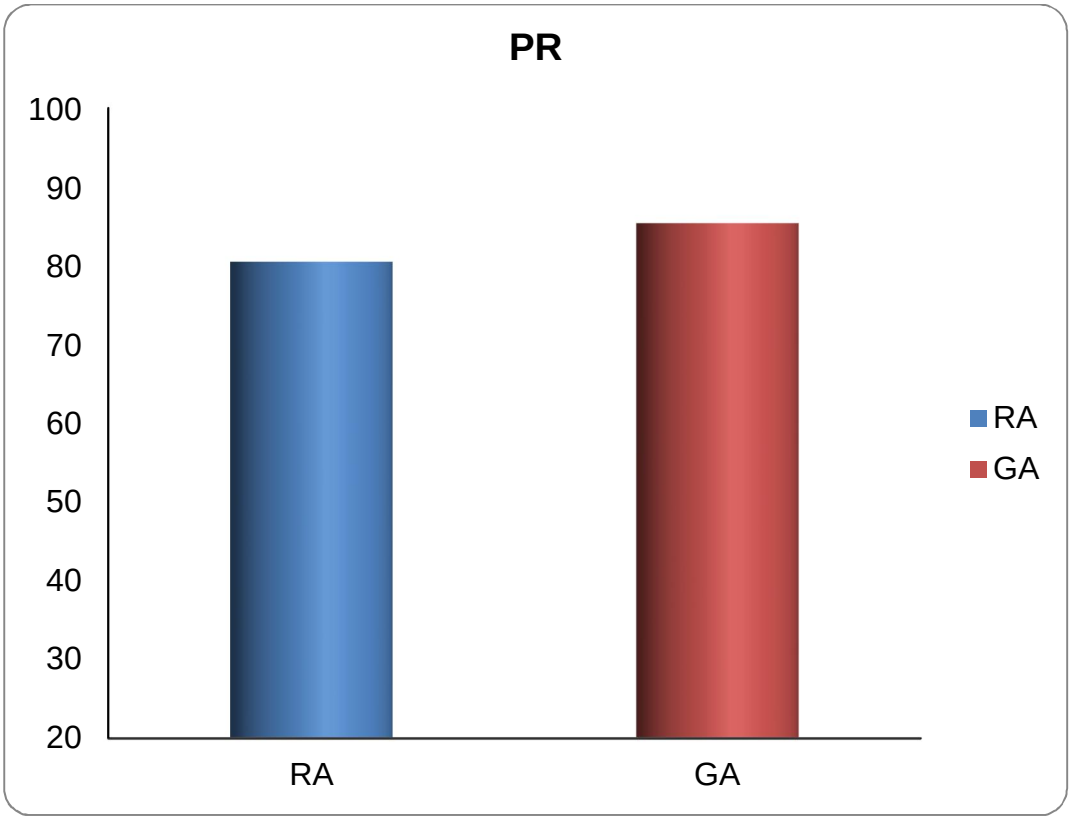


As regards to BMI the two groups are comparable with each other with P value of 0.782

Table 8: Comparison Of Baseline Pulse Rate

Between The Two Groups

Group	RA	GA	P value
Pulse rate	80.55	85.43	0.073

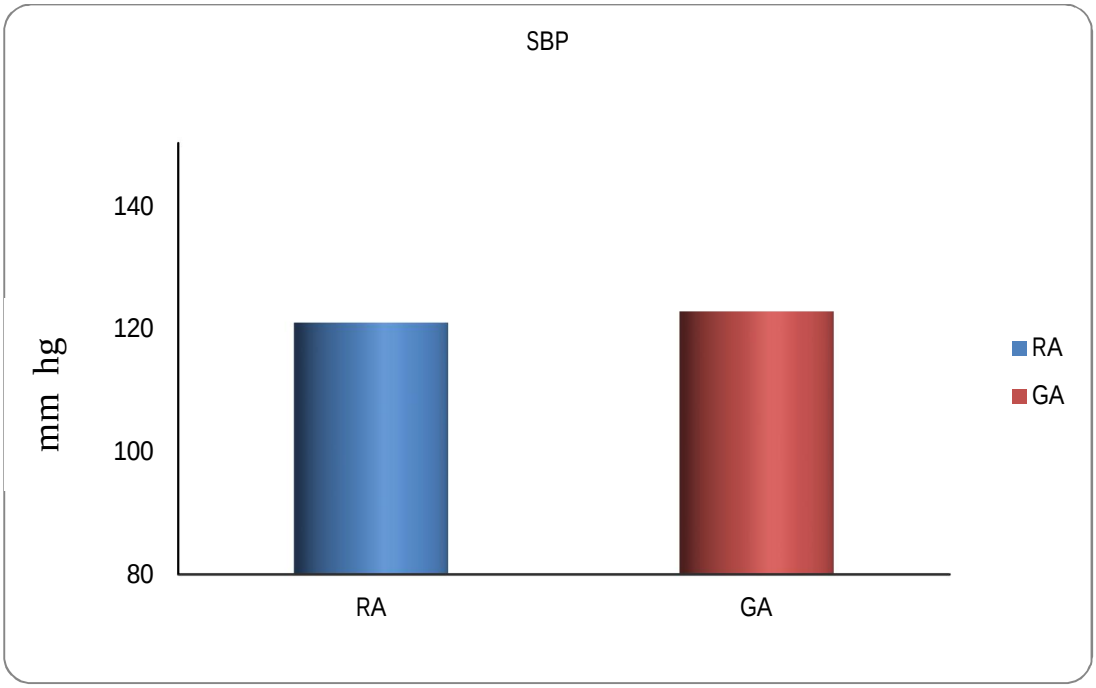


The baseline pulse rate in the two groups are comparable with P value of 0.073

Table 9: Comparison Of Baseline Systolic Blood Pressure

Between The Two Groups:

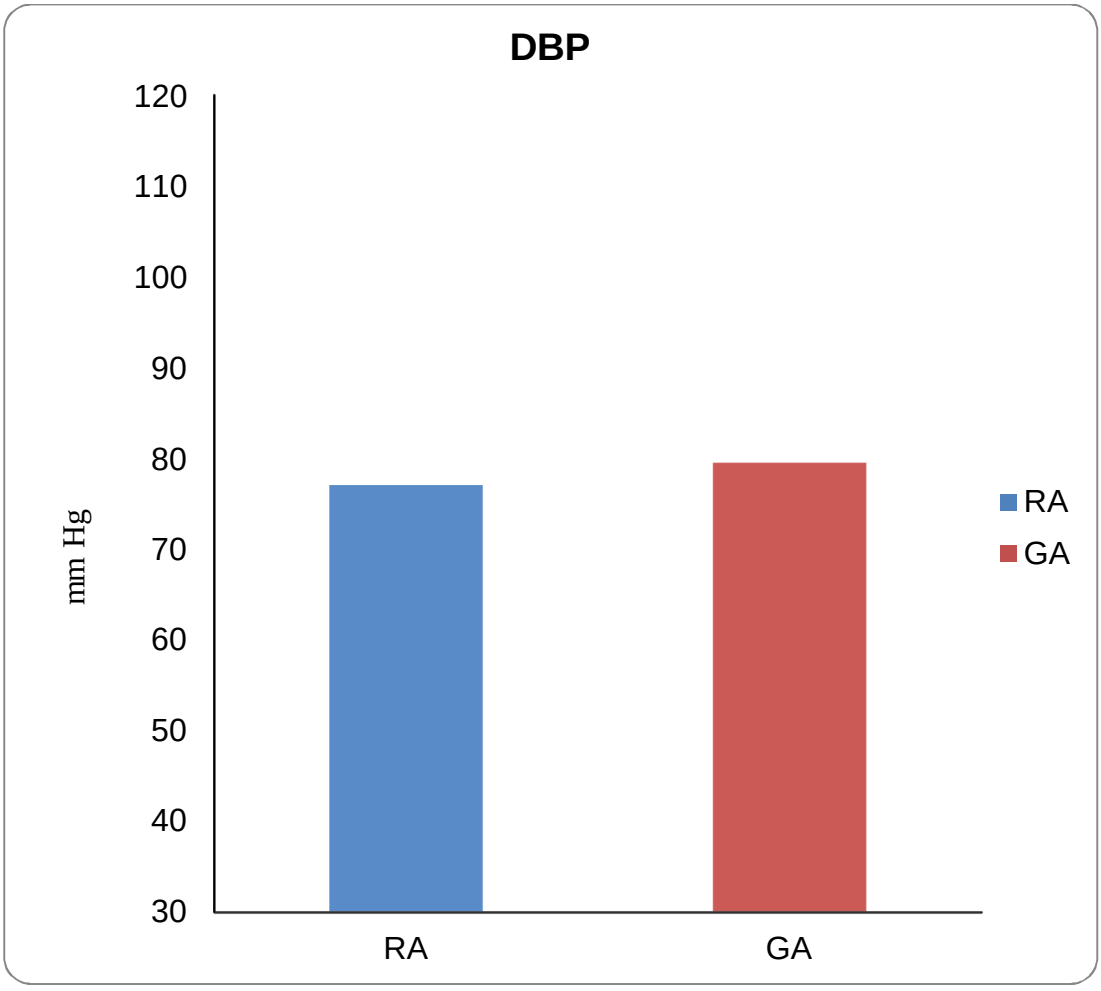
Group	RA	GA	P value
SBP in mmHg	120.87	122.70	0.423



The baseline systolic pressure in both the groups comparable with a P value of 0.423

Table 10: Comparison Of Baseline Diastolic Blood Pressure Between The Two Groups

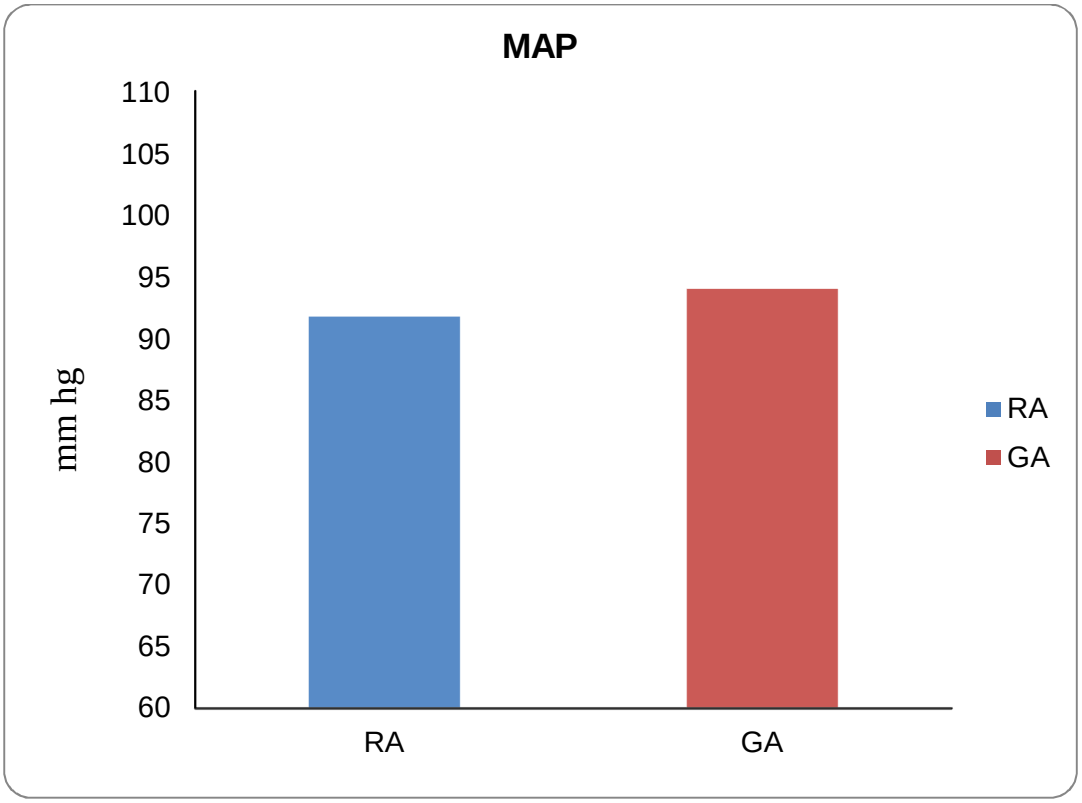
GROUP	RA	GA	P VALUE
DBP	77.19	79.63	0.176



As regards to baseline diastolic blood pressure the two groups are comparable with P value of 0.176

Table 11: Comparison Of Baseline Mean Arterial Pressure Between The Two Groups

Group	RA	GA	P value
MAP	91.75	93.99	0.223

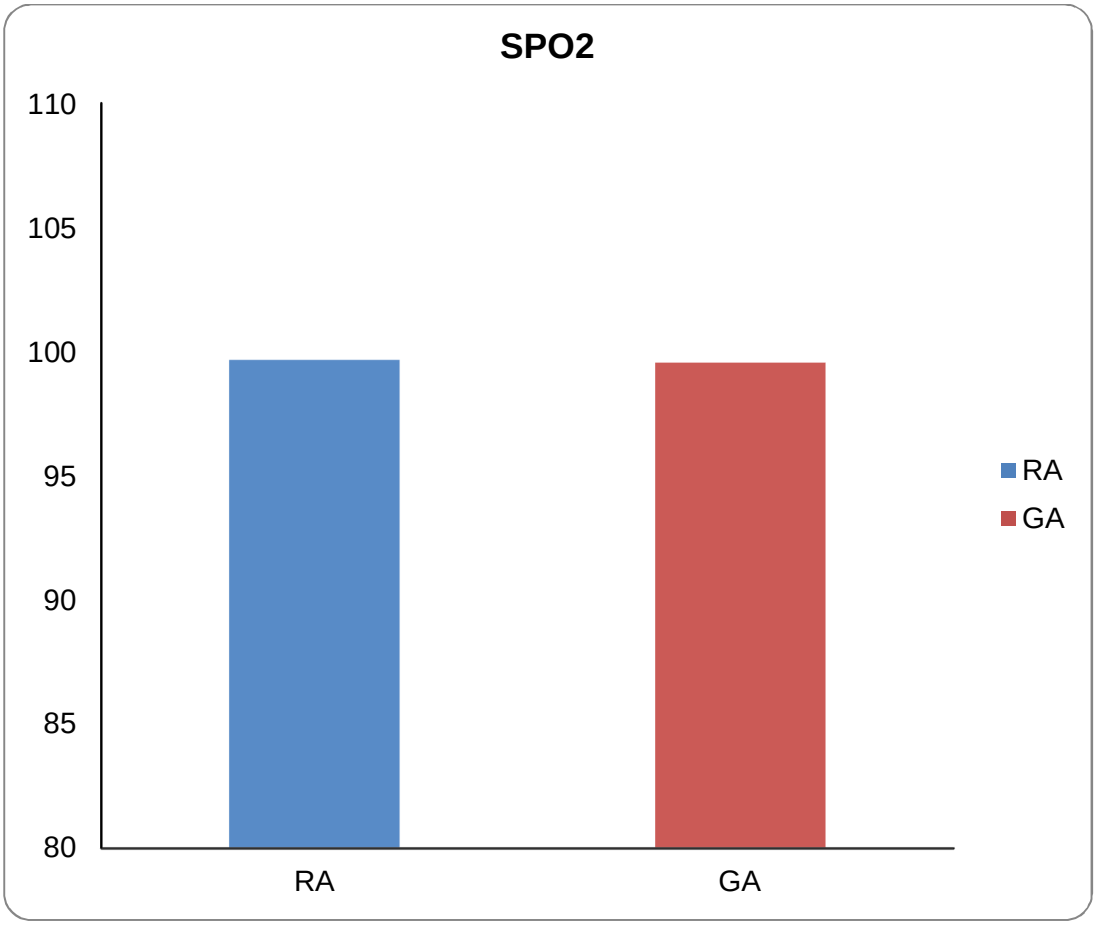


The baseline mean arterial pressure in both the groups are comparable with a P value of 0.223

Table 12: Comparison Of Oxygen Saturation

Between Both The Groups

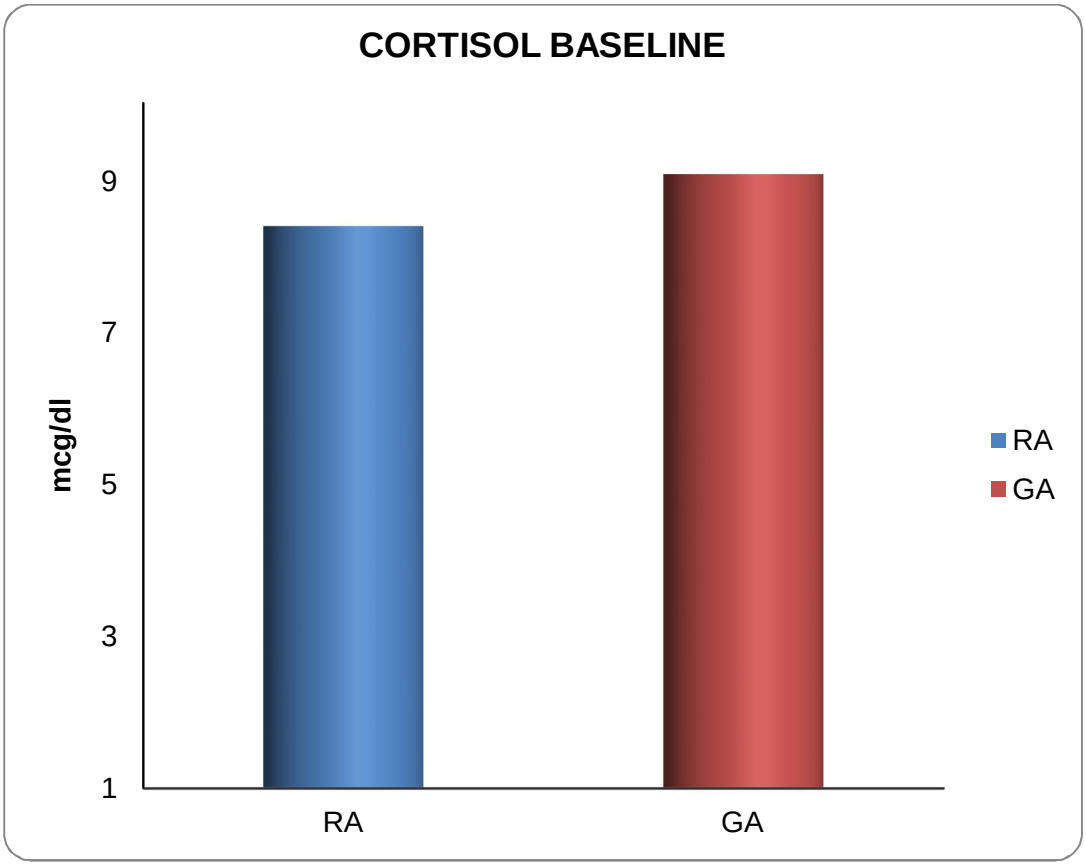
Group	RA	GA	P value
Spo2 in %	99.68	99.57	0.534



As regards to oxygen saturation the two groups are comparable with a P value of 0.534

Table 13: Comparison Of Baseline Cortisol Values

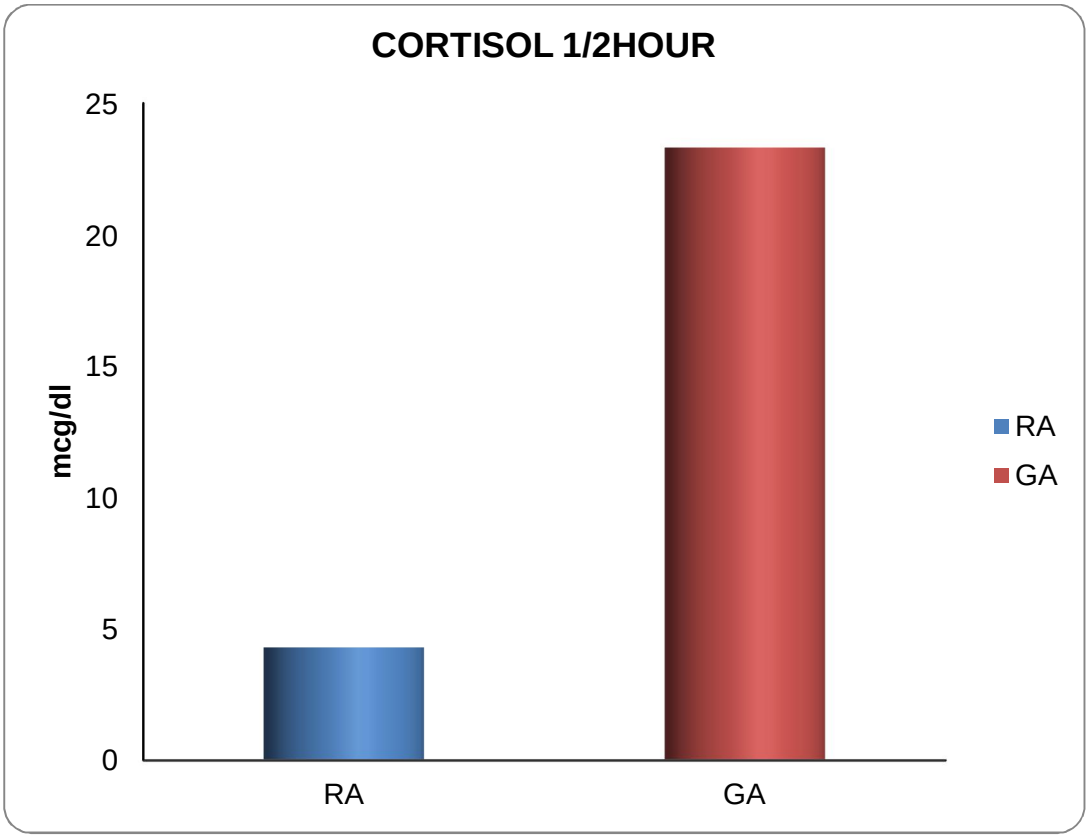
Group	RA	GA	P value
Baseline cortisol in mcg/ dl	8.39	9.07	0.398



The baseline cortisol values in the two groups are comparable with a P value of 0.398

Table 14: Comparison Of Half Hour Cortisol Values

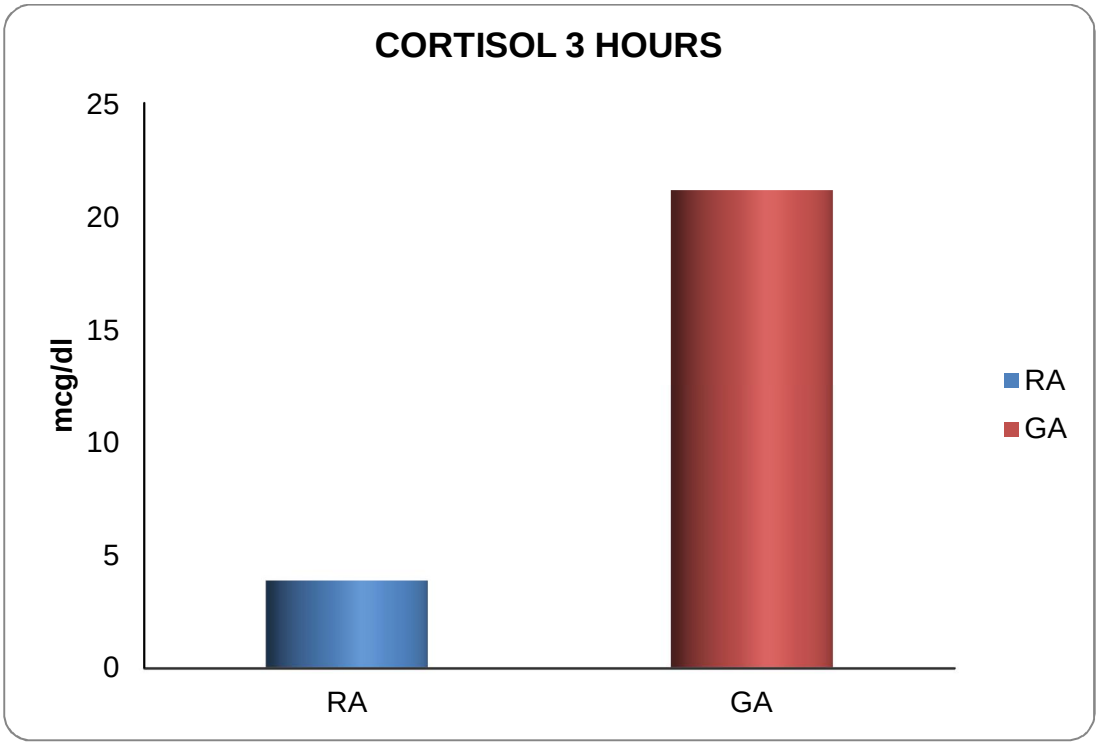
Group	RA	GA	P value
Half hour cortisol in mcg/dl	4.30	23.32	0.0001



The half hour cortisol values was significantly lower in RA group when compared to GA group with a P value of 0.0001

Table 15: Comparison Of Three Hour Cortisol Values:

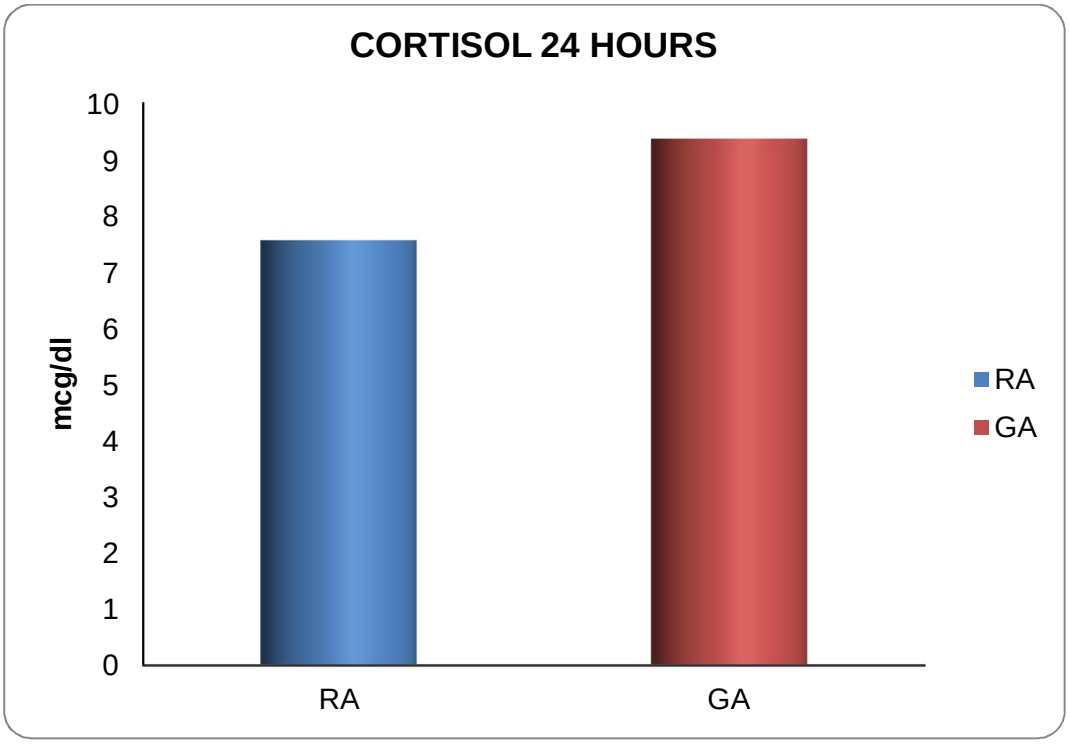
Group	RA	GA	P value
Three hour Cortisol in mcg/dl	3.87	21.16	0.0001



The 3rd hour cortisol values was significantly lower in RA group when compared to GA group with P value of 0.0001

Table 16: Comparison Of Twenty Four Hour Cortisol Values:

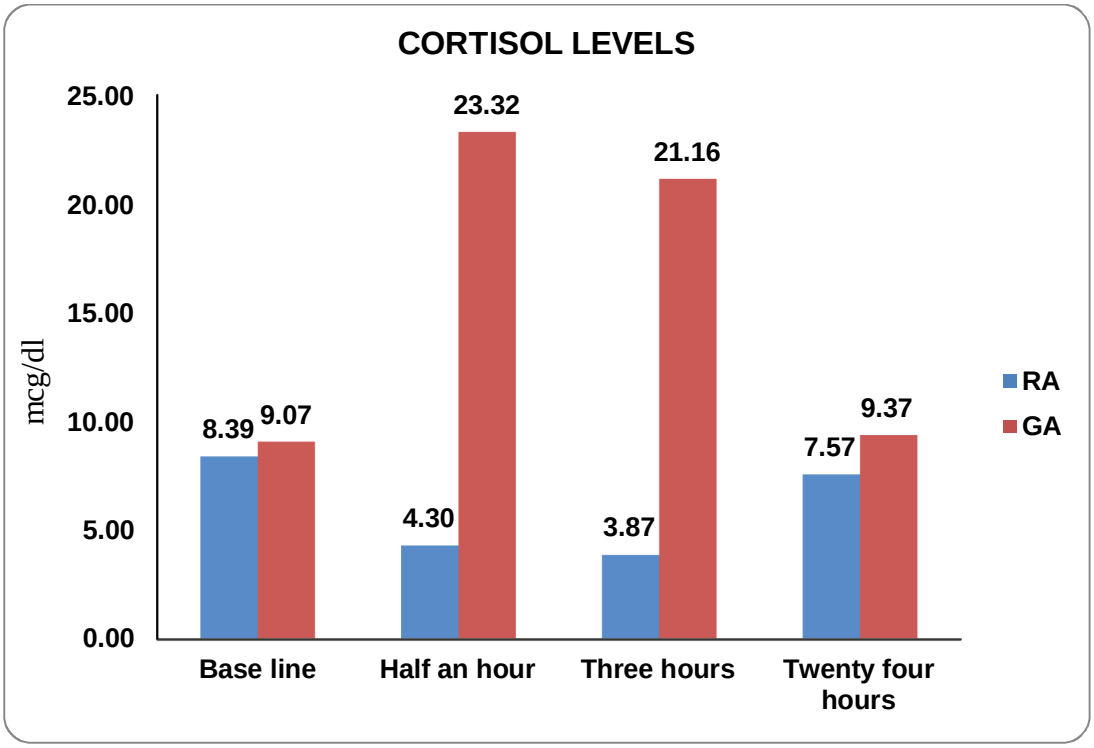
Group	RA	GA	P value
Twenty four hour cortisol in mcg/ dl	7.57	9.37	0.123

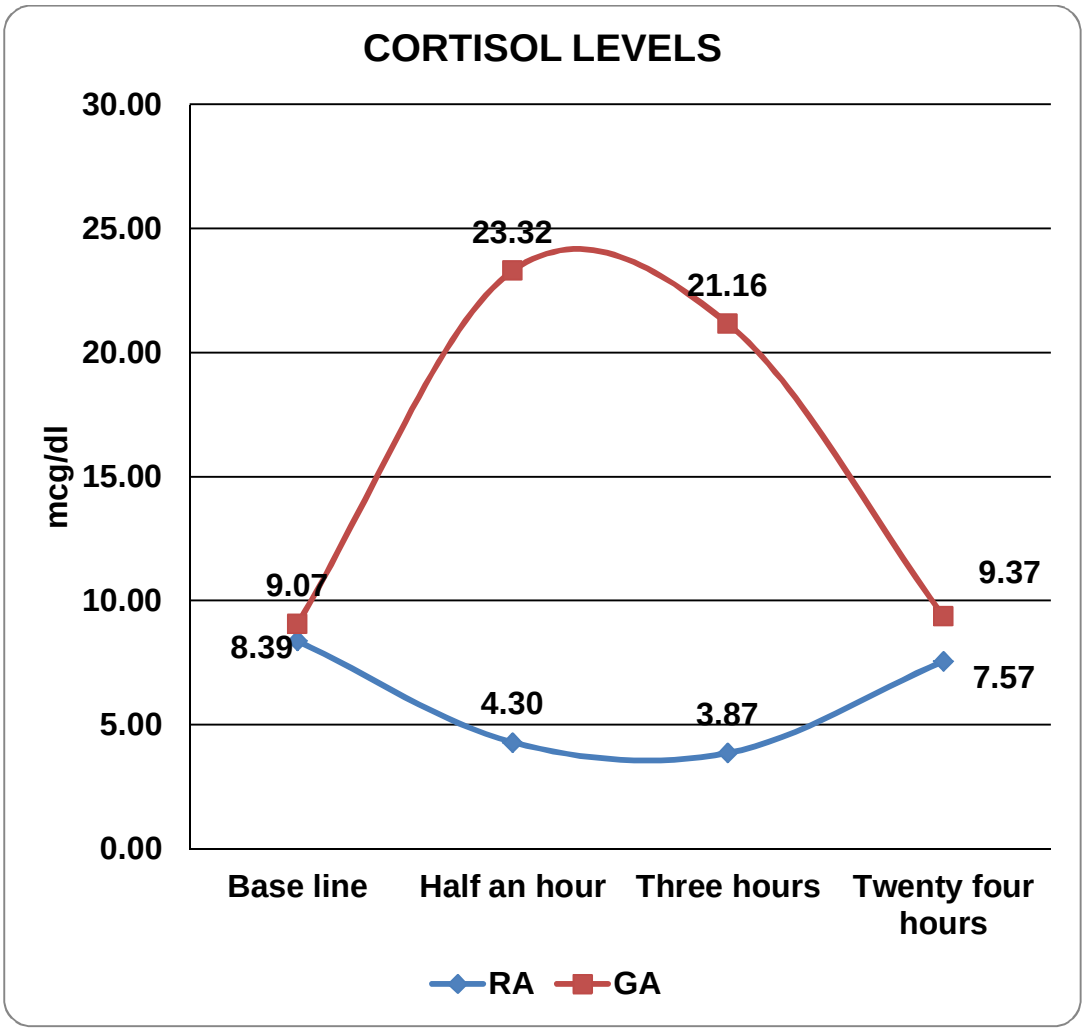


The 24 hour cortisol values in both the groups are comparable with P value of 0.123

Table 17: Comparison Of Cortisol At Various Time Intervals

Group	RA	GA	P value
Baseline cortisol mcg/dl	8.39	9.07	0.398
½ hour cortisol mcg/dl	4.30	23.32	0.0001
3 hour cortisol mcg/dl	3.87	21.16	0.0001
24 hour cortisol mcg/dl	7.57	9.37	0.123




CORTISOL LEVELS
30.00
25.00
20.00
15.00
10.00
5.00
0.00
mcg/dl
23.32
21.16
9.07
9.37
8.39
7.57
4.30
3.87
Base line
Half an hour
Three hours
Twenty four hours
RA
GA

Discussion

DISCUSSION

Cortisol is the most commonly used parameter to assess the stress response to surgery and anesthesia[4]. In our study we compared the serum cortisol levels between patients administered supraclavicular brachial plexus block and general anesthesia for upper limb surgeries. A total of 62 patients were included in the study, 1 patient was excluded from the study due to lysis of blood samples. The remaining 61 patients were divided into two groups, Group RA under supra clavicular brachial plexus block and Group GA under general anesthesia. Blood samples were drawn preoperatively, at ½ hr, 3 hours and 24 hours after skin incision.

The baseline parameters like weight, height, BMI, pulse rate, blood pressure and oxygen saturation were comparable between the two groups. The baseline cortisol levels were comparable between the two groups. Though there was a difference in the cortisol levels at ½ hour and 3 hour samples, the cortisol levels in the 24 hour sample was comparable between both the groups.

Our study showed that the cortisol levels at ½ hour and 3 hours after skin incision was significantly lower in RA group when compared to GA group. The pre operative and 24 hour sample were comparable. This finding was consistent in the study conducted by Aggo et al[4].

The preoperative cortisol levels in both the groups were comparable with P value of 0.398. At 1/2hour the cortisol in Group RA was 4.30±1.59, in group GA was 23.32±14.71. The cortisol values at 3 hours in group RA was 3.87±1.49, in group GA was 21.16 ±12.75. The cortisol values at ½ hour and 3 hour was significantly low in Group RA when compared to Group GA with P value of 0.0001 in both time intervals. At 24 hours the cortisol values were comparable between the two groups with P value of 0.123. This shows that in GA group, skin incision and perioperative period are stressful periods as evidenced by significantly raised cortisol levels when compared to RA group.

In a study by Baker J.P et al[7] the cortisol levels were compared in patients undergoing cataract surgery between patients administered local anesthesia and patients administered general anesthesia.Levels of cortisol were significantly low in local anesthesia group when compared to general anesthesia group.

K Kahveci et al[20] in their study showed that serum cortisol levels were significantly lower in epidural group than in general anesthesia groups for patients undergoing lower limb surgeries.

Surgery associated metabolic and endocrine derangements have a lot of adverse effects which include increased oxygen consumption, catabolism and impaired immune function[3]. These adverse effects may affect the post operative outcome. Clinical evidence has shown that the type of anesthesia might greatly determine the magnitude of stress response. In our study patients undergoing upper limb surgeries were included. Upper limb surgeries are quite common and they are capable of increasing the cortisol levels by increasing the stress response.

Greater than fourfold rise in cortisol levels was seen in general anesthesia group at ½ hour and 3 hours after skin incision when compared to the supraclavicular block group. This difference is due to the fact that in regional anesthesia there is a complete block of sensory, motor and autonomic fibres supplying the area of surgical stimulus[32].

General anesthesia may reduce the perception of surgical stimulus but the sensory inputs from the site of surgery do reach the hypothalamus and produce the various metabolic and endocrine effects of stress response. Intravenous anesthetics, inhalational anesthetics and

opioids do reduce the stress response but only at very high doses which are associated with other potential adverse effects like respiratory depression, post operative nausea and vomiting[(1)(3)]. The normally used doses of these agents have only a minor effect on these stress response.

Regional anesthesia has been shown to directly influence the endocrine and metabolic effects of surgical stress. In supraclavicular nerve block there is complete blockade of nociceptive signals from the surgical site to the hypothalamus. In turn the activation of pituitary by hypothalamus is reduced thereby reducing the levels of ACTH, prolactin etc. this in turn leads to decreased cortisol levels.

This study is in concordance with the above mentioned studies in the fact that cortisol levels were significantly lower in regional anesthesia when compared to general anesthesia. Previous studies are available comparing epidural and spinal anesthesia with general anesthesia. This study was unique in the fact that we compared the cortisol levels in patients undergoing upper limb surgeries between supraclavicular block and general anesthesia.

Summary

SUMMARY

This study was done to compare the serum cortisol levels in patients administered supraclavicular brachial plexus block and patients administered general anesthesia for elective upper limb surgeries.

Surgery is a stressful condition leading to various hormonal, metabolic and immunological changes. These changes have many adverse effects like increased oxygen demand, increased cardiac work, increased chance of infections. All these changes have an effect on the perioperatoive morbidity and mortality. Cortisol is a very sensitive marker of stress response, the magnitude of raise in cortisol depends upon the severity of surgical stress. In this study we compared the cortisol levels between the two groups of patients

In this study a total of 62 patients were included, 1 patient was withdrawn from the study due to lysis of blood sample,the remaining patients were divided into two groups Group GA under general anesthesia with 30 patients and Group RA under supraclavicular brachial plexus block with 31 patients. Both the groups were comparable in terms of baseline characteristics. Venous blood was taken preoperatively, at ½ hour, 3 hours and 24 hours after skin incision. The samples were sent for analysis of cortisol.

The preoperative cortisol levels in both the groups were comparable with P value of 0.398. At 1/2hour the cortisol in Group RA was 4.30±1.59, in group GA was 23.32±14.71. The cortisol values at 3 hours in group RA was 3.87±1.49, in group GA was 21.16 ±12.75. The cortisol values at ½ hour and 3 hour was significantly low in Group RA when compared to Group GA with P value of 0.0001 in both the times. At 24 hours the cortisol values were comparable between the two groups with P value of 0.123.

Conclusion

CONCLUSION

From this study it was concluded that:

Cortisol levels at ½ hour and 3 hours after skin incision was significantly lower in Group RA when compared to Group GA. So the magnitude of stress response was significantly lower in RA group when compared to GA group as indicated by the cortisol level. So it can be concluded that supraclavicular brachial plexus block is better than general anesthesia for upper limb surgeries due to decreased stress response as indicated by the cortisol levels.

Supraclavicular brachial plexues block may also be the anesthetic method of choice in patients in whom the surgical stress may increase the morbidity like in patients with coronary artery disease, elderly, systemic hypertension, diabetes and valvular heart disease.

Bibliography

BIBLIOGRAPHY

1. Desborough JP. The stress response to trauma and surgery. Br J Anaesth. 2000 Jul 1;85(1):109–17.

2. Weissman C. Weissman C. The metabolic response to stress: an overview and update. Anesthesiology. 1990;73(2):308–27.

3. Singh M. Stress response and anaesthesia. Indian J Anaesth. 2003 Dec 1;47(6):427–427.

4. Aggo A, Fyneface‐Ogan S, Mato CN. The differential impact of two anesthetic techniques on cortisol levels in Nigerian surgical patients. Niger J Clin Pract. 2012;15(1).

5. Cruickshank AM, Fraser WD, Burns HJG, Van Damme J, Shenkin A. Response of serum interleukin-6 in patients undergoing elective surgery of varying severity. Clin Sci. 1990 Aug 1;79(2):161–5.

6. Brown DL. Brachial plexus anesthesia: an analysis of options. Yale J Biol Med. 1993;66(5):415–31.

7. Barker JP, Robinson PN, Vafidis GC, Burrin JM, Sapsed-Byrne S, Hall GM. Metabolic control of non-insulin-dependent diabetic patients undergoing cataract surgery: comparison of local and general anaesthesia. Br J Anaesth. 1995 May 1;74(5):500–5.

8. Burton D, Nicholson G, Hall G. Endocrine and metabolic response to surgery. Contin Educ Anaesth Crit Care Pain. 2004 Oct 1;4(5):144–7.

9. Hadzic A, Arliss J, Kerimoglu B, Karaca PE, Yufa M, Claudio RE, et al. A Comparison of Infraclavicular Nerve Block versus General Anesthesia for Hand and Wrist Day-case Surgeries. J Am Soc Anesthesiol. 2004 Jul 1;101(1):127–32.

10. O Riain SC, Buggy DJ, Kerin MJ, Watson RWG, Moriarty DC. Inhibition of the Stress Response to Breast Cancer Surgery by Regional Anesthesia and Analgesia Does Not Affect Vascular Endothelial Growth Factor and Prostaglandin E2: Anesth Analg. 2005 Jan;100(1):244–9.

11. Buyukkocak U, Caglayan O, Daphan C, Aydinuraz K, Saygun O, Kaya T, et al. Similar Effects of General and Spinal Anaesthesia on Perioperative Stress Response in Patients Undergoing Haemorrhoidectomy. Mediators Inflamm. 2006 Feb 9;2006:e97257.

12. Buyukkocak U, Daphan C, Caglayan O, Aydinuraz K, Kaya T, Saygun O, et al. Effects of Different Anesthetic Techniques on Serum Leptin, C-reactive Protein, and Cortisol Concentrations in Anorectal Surgery. Croat Med J. 2006 Dec 15;47(6):862–0.

13. Huiku M, Uutela K, van Gils M, Korhonen I, Kymäläinen M, Meriläinen P, et al. Assessment of surgical stress during general anaesthesia. Br J Anaesth. 2007 Apr 1;98(4):447–55.

14. Sakic K, Zura M, Sakic L, Vrbanovic V, Bagatin D. Neuroimmunomodulation by regional and general anaesthesia. Period Biol. 2009 Jun 15;111(2):209–14.

15. Lakesh Kumar Anand MD, Rohit Jindal MS. Regional anaesthesia for upper extremity in orthopaedics: A review article. Pb J Orthop. 2009;Vol-XI(No.1):1–8.

16. Mirza F, Brown AR. Ultrasound-Guided Regional Anesthesia for Procedures of the Upper Extremity. Anesthesiol Res Pract. 2011 May 30;2011:e579824.

17. Hamada m. Comparitive study between cervical epidural anesthesia and posterior aproach interscaline brachial plexus block in upper limb surgeries. Aamj. 2012 sep;10:403–27.

18. Wafaa g. Ahmed, nuha hamdi. Effects of different anesthetic techniques on inflammatory cytokines response and t - lymphocyte subsets in patients undergoing lower abdominal surgery. Ain shams j anesthesiol. Vol 5-1:43–56.

19. Alimohammadi H, Azizi M-R, Safari S, Amini A, Kariman H, Hatamabadi HR. Axillary Nerve Block in Comparison with Intravenous Midazolam/Fentanyl for Painless Reduction of Upper Extremity Fractures. Acta Med Iran. 2014 Mar 19;52(2):122–4.

20. Kahveci K, Ornek D, Doger C, Aydin GB, Aksoy M, Emre C, et al. The effect of anesthesia type on stress hormone response: Comparison of general versus epidural anesthesia. Niger J Clin Pract. 2014 Jun 24;17(4):523–7.

21. Sadowski M, Tułaza B, Łysenko L. Renaissance of supraclavicular brachial plexus block. Anaesthesiol Intensive Ther. 2014;46(1):37–41.

22. Opperer M, Danninger T, Stundner O, Memtsoudis SG. Perioperative outcomes and type of anesthesia in hip surgical patients: An evidence based review. World J Orthop. 2014 Jul 18;5(3):336–43.

23. Amiri F, Ghomeishi A, Aslani SMM, Nesioonpour S, Adarvishi S. Comparison of Surgical Stress Responses During Spinal and General Anesthesia in Curettage Surgery. Anesthesiol Pain Med [Internet]. 2014 Aug 13 [cited 2015 Sep 6];4(3). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4183098/

24. Das W, Bhattacharya S, Ghosh S, Saha S, Mallik S, Pal S. Comparison between general anesthesia and spinal anesthesia in attenuation of stress response in laparoscopic cholecystectomy: A randomized prospective trial. Saudi J Anaesth. 2015;9(2):184–8.

25. Cruickshank AM, Fraser WD, Burns HJ, Van Damme J, Shenkin A. Response of serum interleukin-6 in patients undergoing elective surgery of varying severity. Clin Sci Lond Engl 1979. 1990 Aug;79(2):161–5.

26. Kaushal RP, Vatal A, Pathak R. Effect of etomidate and propofol induction on hemodynamic and endocrine response in patients undergoing coronary artery bypass grafting/mitral valve and aortic valve replacement surgery on cardiopulmonary bypass. Ann Card Anaesth. 2015 Jun;18(2):172–8.

27. Borgeat A, Ekatodramis G, Schenker CA. Postoperative Nausea and Vomiting in Regional Anesthesia: A Review. Anesthesiology. 2003 Feb;98(2):530–47.

28. Stoelting.R.K, Hillier. S.C. Pharmacology & Physiology in anaesthetic practice. Fourth edition. Philadelphia: Lippincott Williams & Wilkins; Chapter 7, local anaesthetics 179-208 p.

29. Stoelting.R.K, Hillier. S.C. Pharmacology & Physiology in Anesthetic practice. Fourth edition. Philadelphia: Lippincott Williams & Wilkins; Chapter 6, Non Barbiturate intravenous anesthetic drugs, pages 155- 178 p.

30. Butterworth J.F, Mackey D.C, Wasnik J.D. Morgan & Mikhail's Clinical anesthesiology. 5th edition. Mcgraw Hill; Chapter 8, Inhlational Anesthetics, Pages 153- 174 p.

31. Stoelting.R.K, Hillier. S.C. Pharmacology & Physiology in anaesthetic practice. Fourth edition. Philadelphia: Lippincott Williams & Wilkins; Chapter 3, Opioid agonists and antagonists, Pages 42- 86 p.

32. Miller.R.D., Eriksson.L.I, Fleisher.L.A, Wiener- Kronish.J.P, Young.W.L. Miller's Anesthesia. 7th edition. Philadelphia: Churchill Livingstone; 2010. Chapter 52Nerve blocks; p 1640-1644 p.

Appendices

PATIENT CONSENT FORM

Study title : A prospective Randomized controlled study comparing the serum cortisol levels in patients administered general anaesthesia vs supraclavicular brachial plexus block for upper limb surgeries

.

Study centre *: ESIC MEDICAL COLLEGE & PGIMSR,*

K.K.NAGAR, CHENNAI -78

Participant name : **Age:** **Sex***:*

I confirm that I have understood the purpose of procedure for the above study . I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the pitfall in the procedure. I have been explained about the safety,advantage and disadvantage of the techniques. I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that investigator ,regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study . I understand that my identity will not be revealed in any information released to third parties or published , unless as required under the law . I agree not to restrict the use of any data or results that arise from the study .

I understand that that 4 blood samples of 3 ml each will be taken for estimation of the serum cortisol levels. I have been explained that the anesthetic technique is a standard and approved technique. This may help in future research in the field of anesthesia. I consent to undergo this procedure

Insurance No:

Date: *Signature / thumb impression of patient*

X¥òjš got«

1. vd¡F.....mWit á»¢iria brŒíkhW ESIC kU¤Jt® k‰W« FGÉdiu nt©o¡ bfhŸ»nw‹.

2. nehÆ‹ j‹ik :
   á»¢irKiw :

3. vd¡F fG¤âš ku¤J¥ngh»w Cá ngh£L ifia ku¤J¥ nghf brŒaî«. / mšyJ KG ka¡f« bfhL¤J mWit á»¢ir brŒa x¥òjš jU»nw‹.
4. ït‰¿‹ ã‹ÉisîfiskU¤Jt® _y« m¿ªJ¡ bfh©nl‹. nkY« kU¤Jtkid MuhŒ¢á¡fhf 4 Kiw 3ml ïu¤j« vL¤J gÇnrhjid brŒar«kâ¡»nw‹.
5. அனைத்து மருத்துவ சிகிச்சை முறைகளின் நிறைகளும் குறைகளும் எனக்கு விளக்கப்பட்டன..
6. மேலே கொடுக்கபட்டுள்ள அனைத்தும் மருத்துவமனை நன்னெறி (Ethics) குழுவின் வரைமுரைக்கு உட்பட்டே நடக்கும் என மருத்துவர் விளக்கினார். மேலும் இந்த சிகிச்சை முறைகளுக்கு உடன்பட மறுக்கவும் எனக்கு உரிமை உண்டு என்பதை நான் அறிவேன்
7. என் பெயர் உட்பட்ட அடையாளங்கள் மற்றும் நோய் / சிகிச்சை முறை பற்றிய தகவல்களை பிறருக்கு தெரிவிக்கபடாது என மருத்துவர் கூறினார்.
8. என் சிகிச்சையின் போது கிடைக்கும் தகவல்களை மருத்துவ ஆராய்சிக்கு பயன்படுத்தவும் சம்மதம் அளிக்கிறேன்

ehs‹ ïªj x¥òjš got¤ij go¤j ã‹dnu / go¤J¡ fh©ã¡f¥g£l ã‹dnu ïj‹ rhuh«r¤ij KGtJkhf òÇªJ¡ bfh©L ã‹ng KGkdJl‹ r«kâ¤J ifbaG¤âL»nw‹.

rh£á : x¥òjš mË¥gt®

:.....

PROFORMA

Name of the patient: Age:

Sex: Weight:

Insurance No: OT:

Diagnosis: Duration of procedure:

Surgeon: Anesthetist

PREOPERATIVE DETAILS

ASA Grade Remarks:

vitals

BP	Pulse rate	Resp. rate	SpO2	Temp	ECG	Xray

Hb	RBS	RFT	LFT	Others

INTRAOPERATIVE DETAILS:

PROFORMA

Baseline characters	Group GA	Group RA	P value
AGE			
SEX			
HEIGHT			
WEIGHT			

	GROUP GA	GROUP RA	P VALUE
Serum cortisol preop sample			
Serum cortisol 30 minutes sample			
Serum cortisol 3rd hour sample			
Serum cortisol 24hour sample			

SIGNATURE OF INVESTIGATOR SIGNATURE OF THE PARTICIPANT

WITNESS:

KEY TO THE MASTER CHART

1. Group
    a. GA- General anesthesia
    b. RA- Supraclavicular brachial plexus block
2. ASA- American Society Of Anesthesiology Grade
    a. I- American Society Of Anesthesiology Grade 1
    b. II- American Society Of Anesthesiology Grade 2
3. LOS- Level of surgery
    a. I- elbow and above elbow surgery
    b. II- forearm surgery
    c. III- hand surgery
4. BMI- Body mass index
5. PR- Pulse rate
6. SBP- Systolic blood pressure
7. DBP- Diastolic blood pressure
8. MAP- Mean arterial blood pressure
9. Spo2- Oxygen saturation

MASTER CHART

											BASELINE VITALS					CORTISOL VALUES mcg/dl			
S.NO	NAME	GROUP	AGE	SEX	IP NO	ASA	LOS	WEIGHT	HEIGHT	BMI	PR	SBP	DBP	MAP	SPO2	BASELINE	1/2 HOUR	3 HRS	24 HRS
1	NEELAVATHY	GA	58	F	51-23384241	I	I	78	172	26.3656	98	130	90	103.3333	100	15.81	11.02	14.19	0.88
2	SARAVANAN	GA	32	m	510-2345984	II	I	71	169	24.85907	85	115	70	85	100	11.19	16.75	9.13	14.04
3	MUTHU	RA	60	M	51-14689082	II	II	54	160	21.09375	86	125	81	95.66667	100	13.92	4.19	4.62	14.44
4	JEEVA	GA	18	M	51-23472487	I	II	69	170	23.87543	102	126	89	101.3333	98	9.27	21.46	11.65	14.74
5	JANARTHANAN	RA	22	M	51-22838977	I	I	78	176	25.18079	85	105	70	81.66667	99	9	3.4	1.4	6.5
6	THANGAMANI	RA	40	M	51-16728128	I	II	54	156	22.18935	96	110	75	86.66667	100	8.64	4.19	3.64	5.6
7	KANNIAMMAL	GA	46	F	51-20306789	II	II	76	175	24.81633	76	115	75	88.33333	99	8.2	14.7	17	8.6
8	MURUGAN	RA	33	M	51-22667932	I	III	64	157	25.96454	68	118	82	94	100	7.99	4	4.02	0.69
9	SUMATHI	GA	55	F	51-13896291	II	II	68	168	24.09297	78	122	82	95.33333	100	13.8	11.1	15.1	21.1
10	KRISHNA BAHADUR	RA	32	M	51-22228586	I	II	76	174	25.10239	98	115	75	88.33333	100	7.41	3.5	3.3	4.1
11	SIVARAMAN	GA	42	M	51-15170316	I	I	69	176	22.27531	95	125	80	95	100	10.9	13	7.93	12
12	VIVEK	GA	30	M	51-23249675	I	I	58	162	22.10029	78	135	79	97.66667	100	8.2	61.5	25.4	18.4
13	MANIKANDAN	RA	28	M	51-22023054	I	II	58	162	22.10029	76	132	85	100.6667	98	9.87	3.51	2.41	8.4
14	RAMESH	GA	37	M	51-49383241	I	I	75	179	23.40751	105	135	91	105.6667	99	5.19	14.4	17.3	5.3
15	SELVAM	GA	52	M	51-23563655	II	I	60	172	20.28123	110	132	82	98.66667	99	10.5	14.6	16.7	6.5
16	THILAGAVATHY	RA	43	F	51-12241514	II	II	62	165	22.77319	95	130	80	96.66667	100	7.41	2.64	5.2	8.23
17	MOHAN	GA	36	M	51-11721474	I	II	66	169	23.10843	85	135	85	101.6667	100	5.02	13.5	14	12.9
18	JESUDOSS	RA	46	M	51-11964384	I	II	58	158	23.23346	79	120	80	93.33333	100	9.39	3.9	2.9	8.09
19	PALANI	GA	40	M	51-20468674	I	II	66	172	22.30936	78	121	85	97	100	4.34	11.5	13.6	5.8
20	CHRISTOPHER GEROGE	GA	45	M	51-20537532	II	I	64	164	23.79536	72	120	82	94.66667	100	15.7	12.5	11	2.89
21	RENUKA	RA	60	F	51-17587415	II	I	64	164	23.79536	89	120	80	93.33333	97	7.58	4.72	5.3	2.75
22	NARESH BAHADUR	GA	35	M	51-23789456	I	II	70	168	24.80159	84	115	62	79.66667	99	5.25	12.2	11.6	10.65
23	CHINNA	RA	42	M	51-21303162	I	II	70	174	23.12062	85	125	86	99	100	7.77	2.3	3.5	10.5
24	NARENDRA KUMAR	GA	41	M	51-43645239	I	III	71	169	24.85907	96	123	89	100.3333	100	8.56	20.5	15.6	15.5
25	RAJALAKSHMI	GA	54	F	51-15379502	II	I	65	162	24.76757	97	126	82	96.66667	99	7.86	20.6	13.21	7.7
26	AADHI LAKSHMI	GA	39	F	51-29322116	I	II	58	162	22.10029	85	139	85	103	100	19.5	20.5	21.27	7.92
27	RAJKUMAR	RA	21	M	51-32411964	I	II	72	165	26.44628	65	130	82	98	100	8.2	7.5	6.2	22.5
28	GANAPATHI	RA	50	M	51-17255306	I	I	52	158	20.83	72	113	70	84.33333	98	7.64	3.84	5.45	7.65
29	KAMAL	RA	25	M	51-22100183	I	II	62	159	24.52435	76	135	81	99	100	9.62	4.22	1.45	1.47
30	UPENDRA KUMAR	GA	49	M	51-14778423	II	II	79	176	25.50362	84	122	75	90.66667	99	9.38	60.5	60.6	6.06
31	JAGADESHWARI	GA	32	F	51-15129466	II	II	68	167	24.38237	75	112	72	85.33333	100	3.02	61.5	21.3	2.4
32	RAJKUMAR	RA	25	M	51-20719280	I	II	79	165	29.01745	69	105	65	78.33333	100	7.2	0.43	1.51	5.63
33	ARUN KUMAR	RA	23	M	51-22807569	I	II	72	171	24.62296	65	105	69	81	100	10.5	7.23	4.74	9.6
34	VIJAYA KUMARI	GA	51	F	51-17500450	II	II	66	162	25.14861	75	113	70	84.33333	99	13	25	23	1.19
35	JAYARAMAN	GA	50	M	51-17689422	II	II	72	172	24.33748	85	115	75	88.33333	100	2.6	44	61.5	1.51
36	ANANDHAN	RA	38	M	51-22801803	I	II	69	168	24.44728	75	121	79	93	100	8.65	5.22	4.44	2.66
37	GOPINATH	RA	19	M	51-15585981	I	II	67	168	23.73866	85	113	70	84.33333	100	9.58	6.32	5.82	6.29
38	RAJESH	RA	23	M	51-27849321	I	II	74	176	23.88946	78	110	69	82.66667	100	5.41	3.12	2.01	3.66
39	PURUSHOTHAMAN	RA	23	M	51-23207087	I	II	70	169	24.50895	88	119	82	94.33333	100	4.74	5.31	2.94	11.1
40	LATHA	RA	34	F	51-22496545	I	II	76	178	23.98687	87	129	79	95.66667	100	3.11	4.34	1.56	4.21

41	SIVAGANAPATHY	GA	21	M	51-24577656	I	II	69	174	22.79033	90	125	85	98.33333	100	6.06	11.2	8.59	10.2
42	MUGUNDHAN	GA	52	M	51-21071235	I	II	69	172	23.32342	92	122	86	98	98	8.26	25.26	30.25	10.25
43	PARTHIBAN	RA	32	M	51-16894427	I	II	70	171	23.93899	82	126	80	95.33333	100	7.14	2.12	3.15	8.65
44	GEETHA	RA	40	F	51-16684666	II	I	69	170	23.87543	102	140	89	106	100	10.25	3.25	2.56	8.15
45	BASKARAN	GA	33	M	21-21665549	I	II	80	177	25.53545	79	122	82	95.33333	100	5.62	25.2	26.5	8.55
46	ARUN KUMAR	RA	23	M	51-21510291	I	II	62	168	21.96712	75	135	94	107.6667	100	6.25	4.26	3.65	6.98
47	MANAS KULI	RA	20	M	51-23483762	I	II	64	163	24.08822	85	126	75	92	100	7.56	2.56	2.65	7.56
48	ARUN NEWTON	RA	25	M	51-24586955	I	I	72	168	25.5102	80	122	71	88	100	8.56	5.23	5.11	8.21
49	ANANDHI	GA	32	F	51-11296012	II	I	68	164	25.28257	95	120	80	93.33333	100	9.56	29.82	36.52	13.55
50	SEKAR	GA	47	M	51-22494976	I	I	65	169	22.75831	88	113	72	85.66667	99	8.44	30.52	21.56	10.22
51	PADMANABAN	GA	33	M	51-16310385	I	I	63	157	25.55885	78	125	80	95	100	9.25	19.5	17.2	10.11
52	PARTHIBAN	RA	45	M	51-15151359	II	II	67	178	21.14632	65	112	70	84	100	8.06	5.16	6.15	7.01
53	USHA MAHESHWARI	GA	52	F	51-20313353	II	I	70	168	24.80159	78	130	80	96.66667	100	7.56	21.56	25.63	11.2
54	AMUTHAVALLI	RA	41	F	51-22998000	I	II	69	174	22.79033	88	133	77	95.66667	99	9.99	5.26	6.11	8.22
55	GEORGE	RA	52	M	51-16383403	I	II	69	165	25.34435	75	132	75	94	100	7.55	4.25	3.56	8.25
56	SURENDAR	RA	29	M	51-24383336	I	II	64	164	23.79536	71	111	64	79.66667	99	8.22	5.26	5.14	8.31
57	ARUN KUMAR	GA	23	M	51-215C6291	I	II	71	168	25.1559	79	123	81	95	100	11.26	22.56	25.65	11.56
58	PALANI	GA	40	M	51-23306496	I	I	66	164	24.53896	62	115	75	88.33333	100	9.54	16.5	19.66	11.25
59	VASUDEVAN	RA	35	M	51-23238957	I	II	64	159	25.31545	69	115	80	91.66667	100	9.23	4.25	4.99	9.45
60	VISHNU	GA	19	M	51-13230821	I	I	62	155	25.80645	79	110	68	82	99	9.23	16.52	22.26	8.23
61	MANI	RA	40	M	51-15062586	I	II	69	166	25.03992	88	115	78	90.33333	100	13.77	7.88	4.54	9.76